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# CLINICAL MEDICINE



JANUARY, 1954

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PREGNANCY TEST  
POWDERED MILK FORMULA  
ACUTE INTUSSUSCEPTION  
CIRRHOSIS OF THE LIVER  
OFFICE GYNECOLOGY  
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Literature available on request. Write Medical Service Division, Ciba Pharmaceutical Products, Inc., Summit, N.J.

1. SIMON, S. W. : ANN. ALLERGY 51:128, 1955. 2. KESTEN, D. M. : ANN. ALLERGY 6:402, 1948. 3. LOEW, E. R. : MED. CLIN. N. AM. 36:1551, 1940.

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## 60 years of Medical Journal Publishing

*The original, January 1, 1894  
editorial page of The Alkaloidal Clinic  
is reproduced on page 24*

---

JAMES M. NORTHINGTON, M.D., *Editor*

The *Alkaloidal Clinic* of some 35 years ago, a forerunner of *Clinical Medicine*, brings to mind vivid and pleasant recollections. That journal exercised a wholesome influence in getting for the patient exact dosage of potent remedies and in lessening the use of "shot-gun" prescriptions, of which only the Lord knew the action.

Two of the liveliest of these recollections are one of an article on "Lues the Incurable", the other entitled, "One Inch, One Minute, One Day." The former was a powerful plea for telling patients and public that syphilis could not be cured. It concluded with: "Shake the mumbling mask of paresis, or the dangling legs of tabes before him, and the most hardened voluptuary will be startled." The other was the description by some surgeon of how

he removed the appendix vermiciformis in one minute through a one-inch incision, and kept the patient in the hospital one day.

An article, "Too Many Medical Journals," in *Medical Economics* (August, 1953), repeats the plaint made in the first paragraph of Dr. Abbott's editorial of 60 years ago. Whether or not there are too many medical journals is a moot point. That there are too many medical articles, that most of them are too long, and that many of them are of little or no practical value to anybody—this is certainly true. I have read many that brought to mind the criticism an old Scottish elder made of a sermon by the trial minister: "In the first place, ye read it; in the second place, ye didn't read it well; in the third place, if ye had spoke it, and spoke it well,

# THE ALKALOIDAL CLINIC.

Vol. I.

JANUARY, 1894.

No. 1.

## THE ALKALOIDAL CLINIC

*A Monthly Journal Devoted to Accuracy in Therapeutics, with Practical Suggestions Relating to the Clinical Application of the same.*

W. C. ABBOTT, M. D.,

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OUR AIM is to make this journal an informal interchange of thought and experience between those interested in Alkaloidal medication.

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### A WORD OF EXPLANATION.

In view of the great number of medical journals that claim attention, covering every locality, and every seeming need of the profession, while in some sections, principally in the East, they pile up mountain high, it may seem presumptuous for us to place THE ALKALOIDAL CLINIC before you, expecting a hearty reception.

For some years there has been a widespread demand for current literature devoted to discussion of the ways and means of alkaloidal medication. We hoped much from *The Alkaloid*, the first attempt in that direction, and, while in no way connected therewith other than as a subscriber and well wisher, lent it our earnest support. After an existence of some months it gradually lapsed into a state of somnolence from which it never yet has been aroused.

During the uncertain life of *The Alkaloid* came another, *The Alkaloidal Clinic*, which again revived hope in the hearts of those wishing light and help on this subject. The life of this was even shorter than the other, and it expired before it cut its first teeth.

Liking this latter name, as it clearly defines the ground we aim to cover, we have adopted it, with the consent of the originators, for this journal, to which we respectfully call your attention.

### SUBSCRIBERS.

THE ALKALOIDAL CLINIC goes to a few hundred supporters this month, and, as a courtesy, to some thousands more. Many of these latter, we hope, will be subscribers before our next issue. With the exception of now and then a sample copy, THE ALKALOIDAL CLINIC will only be sent as paid for, so it behooves a reader who sees this issue and wishes to see more, if he be not a subscriber, to act now. We are so confident of the interest you will feel in the matter we have to give you, that we will send you the journal three months on receipt of 30 cents in stamps, or, if you will send \$1.00 for 1894 and are not satisfied with your investment after you have read three numbers, we will refund your money entire on receipt of the three journals and a statement from you to that effect.

### OUR POSITION.

We compete for recognition with none as we believe we have a little niche as yet unoccupied. We aim to be as helpful as possible to all who take an interest in this work. We believe that with this issue we give you valuable ideas, and our friends who have helped us this time have many more good things for these pages. Let us have help from all.

it wouldna' been worth listening tae."

The editor of any journal that is the "official organ" of any body of doctors is unable to exercise proper discretion as to the publishing of papers read before the annual meetings. Few program chairmen dare reject an offer of a paper from a member. Nothing more need be said in explanation of why so much of what is called "medical literature" is such poor stuff. A few years ago one of the best of our State Medical Journals announced that no more long bibliographies would be published, but the practice has been resumed. The pressure was too great. Long bibliographies are all right for monographs, but they have no legitimate place in an article for busy doctors trying to keep up with the latest on diagnosis and treatment that has been *proved* useful. The big joke about bibliographies is that not one author in a dozen looks them up himself and not one-fourth of them can read a sentence of the French, German, Spanish or Italian articles they cite.

The English historian of the last century, Froude, is credited with having said: "The knowledge that one can use, that converts itself into practical power is the only real knowledge: all the rest hangs like cobwebs on the brain, or dries like raindrops off the stones." What could be truer? How a certain test or drug was worked out and by whom, has nothing to do with serviceability to patient and doctor. It takes a keen and diligent mind to keep up with the essentials of medical advances. There is no time for

the superfluities. It may gratify the egotism of a writer to copy down a 150-word formula—five minutes later he could not repeat it for his life. This only irritates the doctor trying to get something useful out of the article. Finally—and this is an open secret—specialists rarely read anything about any part of medicine other than their specialty, and then rarely more than summaries.

The reason why doctors pay money for independent journals when they get others along with their memberships is that the editors of the former seek and accept articles for their usefulness, and edit out the redundancies.

Every contributor to the pages of *Clinical Medicine* is asked to put himself in the place of a reader and write nothing he would not like to read and consider well worth the time expended. Leave out "approximately." The world is not exactly 25,000 miles in circumference, but that is close enough. Don't write "secure" when "procure," "obtain," or even 3-letter "get" is the word for the place.

Finally, don't use the word *case* when you mean *patient*, or vice versa. No clergyman fails to distinguish between the *case* of his parishioner and the parishioner *himself*. No lawyer confuses the *case* of his client with the client's *person*. We, in the medical profession, must likewise think, speak, and write in a way that will justify our position. Osler spoke in high praise of the dictionary as a book for doctors to use.





"It's so good to be back  
on the job, doctor"

TABLET

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## Facts and Fancies About Cancer of the Lung

*The startling rise in the recorded death rate from lung cancer may be due to changes in numbers and age of the population and to improved diagnosis*

JAMES M. NORTHINGTON, M.D., *Editor*

Under this title, D. W. Smithers, M.D., Director of the Radiotherapy Department of the Royal Cancer Hospital, London<sup>1</sup>, writes a thoughtful, informative, and in some ways startling, article. Certainly, I never thought of primary lung cancer as other than a very rare disease until after World War I; and if any member of either of the first-class faculties with which I had been on intimate terms knew anything to the contrary, he kept it to himself.

Yet, here comes a learned English doctor with proof that two eminent authorities<sup>2</sup> had put it on record, in a world-renowned medical publication, the deaths from lung-cancer were being registered in increasing numbers in 1893; and that, in 1912, another eminent authority<sup>3</sup> wrote a monograph, "attacking the current

opinion that cancer of the lung was rare!"

The following paragraphs carry the substance of what Smithers says further:

King and Newsholme<sup>2</sup> in 1893 were maintaining that the registered increase in cancer deaths was due to improved diagnosis and better death certification. Adler<sup>3</sup> in 1912, in his famous monograph, attacked the current opinion that malignant neoplasm of the lung was rare and maintained that this was a common disease which a physician might meet "any day in his practice amongst the young as well as

1. Smithers, D. W., *British Medical Journal*, June 6, 1953.

2. King, G., Newsholme, A., *Proc. Royal Society*, 54:209, 1893.

3. Adler, I., *Primary Malignant Growths of the Lung & Bronchi*, Longmans, Green & Co., New York & London, 1912.

amongst the old."

Doctors in England and Wales by 1949 were writing "cancer of the lung" on death certificates 25 times more often than they had been doing in 1912. There is no doubt today that the lung is one of the commonest sites in the human body for primary as well as for secondary malignant disease. It is clear that some real increase in lung cancer has occurred in many parts of the world. What is not at all clear is the extent of that increase.

Much of the recorded rise can be accounted for. The number of persons living in England and Wales has gone up by  $7\frac{1}{2}$  millions in the past 40 years; and 21 persons in every 100 alive today are over 55 years of age, while only 12 persons in every 100 were over 55 then. In this country in this period the number of persons per doctor has been reduced from 1400 to 900. The death rate from cancer as a whole has been increasing over the years, cancer of the lung having shown the most spectacular rise.

It was not until the 1930s that bronchoscopy became a common form of examination even in special chest hospitals. At the Brompton Hospital bronchoscopic examinations done in 1930 numbered 28, while the number today is over 800, per annum.

More patients now recover from chest infections which may be associated with a bronchial carcinoma. The immense increase in radiological examination of the chest has been another important factor in the diagnosis of bronchial tumours. The most rapid increase in registration of lung cancer deaths did not, in

fact, occur until the modern facilities for diagnosis of this disease became generally available. Even today the accuracy of the diagnosis of bronchial carcinoma in the country as a whole and the reliability of death certification from this cause must still be under grave suspicion.

The startling rise in the recorded death rate from lung cancer is in large part due to change in numbers and age of the population and to improved diagnosis. It is due in part to a real increase, but we are not yet in a position to say how great that real increase is.

Some 90,000 people are dying each year with lung symptoms. We should ask ourselves how far we are performing a useful service by helping to make a public issue of a comparatively small change within that group, which may be in large part due to our own method of recording. We should not be too readily swayed by those who demand that the public "be told the truth," while we are still attempting to sort the facts from the fancies for ourselves, especially since "the truth" when told may not appear to them in at all the same light as it does to us.

Who among us would question the soundness of his concluding paragraphs?

"As a profession which speaks so much and so rightly of the need to allay the cancer fear, we should beware of putting extravagant accounts of rising cancer death rates and their causes before the public, especially when neither the magnitude of the one nor the degree of responsibility of the other has yet been fully established."



## Treatment of Parkinsonism

*Emotional rehabilitation must complement the therapeutic regime if treatment of this progressive disease is to be successful*

---

S. K. SHAPIRO, M.D., Division of Neurology, University of Minnesota and Mount Sinai Hospitals, Minneapolis, Minnesota

Parkinsonism is a chronic progressive disease, characterized chiefly by tremor and rigidity. To date there is no therapy which can remedy or halt the progressive pathological changes in the central nervous system which are responsible for this condition. All therapies are of necessity symptomatic. The use of all drugs we have effects a 40 to 50% improvement in the symptoms under optimum conditions. Careful consideration must be given to the emotional features of each case to obtain the most satisfactory adjustment possible. It is not sufficient to give the patient a hastily written prescription and expect that he will do well.

Intensive formal psychotherapy is required in few cases; practical sympathetic approach is necessary

to the patient as a whole. When the diagnosis has been established, a frank discussion should be had with the patient about the nature of his condition. He should be told that his disease involves the central nervous system and that the damaged areas of the brain can not be repaired, that most patients with parkinsonism live a normal life span and that within certain limitations he can continue his life as formerly. He must expect certain limitations of his activities, exercise and activity just short of fatigue, he is told that this condition will never effect his mentality, that his disease will never paralyze him, and that any difficulty in motor function is due to rigidity and not paralysis. Many patients derive great emotional support from this reassurance. At subsequent visits direct the patient's

interest into occupational and recreational pursuits within his capacity. Families must be cautioned against rushing the patient and to allow him to maintain the feeling of independence which comes from things for himself. These patients frequently become demanding and overbearing and require firm management. The emotional problems of each patient must be dealt with as they arise.

Against the background of continuous emotional support, drug therapy can be expected to give an additional 40 to 50% improvement. It is frequently necessary to try many different drugs or combination of drugs, before the ideal drug therapy is reached for the individual patient. No one preparation is clearly superior to others. One may develop a tolerance to medication which has formerly produced a good result, making necessary a change in medication. A minimum period of 6 months is required for determining if a drug has a beneficial effect.

The psychotherapeutic effects of a change in medication are such that the patient on placebos can demonstrate objective improvement for a period of up to 5 months. Any improvement from a drug maintained after the 6 months period is in all probability due to the effect of the drug. The medications currently available will be considered in more detail.

#### BELLADONNA DÉRIVATIVES

Drugs of this group are still the mainstay of drug therapy in parkinsonism. The active alkaloids of the belladonna group used are atropine, scopolamine (hyoscine), and hyoscyamine. Tincture of stromonium is used occasionally and contains atropine and hyoscyamine. Others of the group are bellabulgar, rabellon and

vinobel, containing varying proportions of atropine, scopolamine and hyoscyamine. Each tablet of bellabulgar (Lederle) contains 0.4 mgs. of the total alkaloid of belladonna. Rabellon (Sharpe and Dohme) is a 0.5 mg. tablet—0.45 mgs. hyoscyamine, .037 mgs. atropine and 0.012 mgs. scopolamine. Vinobel (Merrill) tablets are of two sizes: 0.4 mgs. (red) and 0.8 mgs. (orange) tablet.

The toxic symptoms produced by these drugs are dryness of the mouth, urinary retention, visual blurring, nausea, diarrhea and constipation; and central nervous system symptoms such as headaches, dizziness and in some instances confusion, delirium, and hallucinations.

Rabellon, vinobel, bellabulgar, and to a lesser extent hyoscine and atropine, are the drugs of this group which are largely being used. Tincture of stromonium is of benefit in the occasional case. Atropine is particularly useful where salivation is troublesome.

Initially one must determine the maximum dosage that the patient can tolerate, and then the minimum dosage which produces maximum therapeutic effect. This is the maintenance dose of the drug. Table 1 illustrates the scheme which is used in the administration of rabellon. A similar schedule is followed when the other drugs are prescribed. The maximum dose is given before retiring so that any toxic symptoms will occur at the time when they will cause a minimum of discomfort. It is difficult to fractionate the bellabulgar and vinobel tablets and it is customary to prescribe one tablet as an initial dose and one tablet every second or third day until a suitable schedule has been worked out.

Atropine is administered in a 0.5% solution commencing with 1 drop; t.i.d. and increasing to 10 drops

Table 1—RABELLON SCHEDULE

Rabellon Tablets—.5 mg. each

Days	A.M.	Noon	Bedtime
1	$\frac{1}{4}$	$\frac{1}{4}$	$\frac{1}{2}$
2	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$
3	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{3}{4}$
4	$\frac{3}{4}$	$\frac{3}{4}$	$\frac{3}{4}$
5	$\frac{3}{4}$	$\frac{3}{4}$	1
6	1	1	1
7	1	1	1
8	1	1	$1\frac{1}{4}$
9	$1\frac{1}{4}$	1	$1\frac{1}{4}$
10	$1\frac{1}{4}$	$1\frac{1}{4}$	$1\frac{1}{4}$
11	$1\frac{1}{4}$	$1\frac{1}{4}$	$1\frac{1}{2}$
12	$1\frac{1}{2}$	$1\frac{1}{4}$	$1\frac{1}{2}$
13	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{1}{2}$
14	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{3}{4}$
15	$1\frac{3}{4}$	$1\frac{1}{2}$	$1\frac{3}{4}$
16	$1\frac{3}{4}$	$1\frac{3}{4}$	$1\frac{3}{4}$
17	$1\frac{3}{4}$	$1\frac{3}{4}$	2
18	$1\frac{3}{4}$	2	2
19	2	2	2

Increase thereafter by  $\frac{1}{4}$  tablet daily. If any toxic symptoms occur, such as excessive dryness of mouth, dizziness or blurring of vision, return to dosage of previous day for one week and then attempt to increase again. An attempt is made to maintain maximum dosage without untoward symptoms.

1/100 or 1/150 in a manner similar to bellabulgar and vinobel. Tincture of stramonium is started with 20 drops, t.i.d. and slowly built up—usual maintenance dosage 60 drops t.i.d.

#### ARTANE

In general, the reactions of artane resemble those of atropine. However, it is entirely free from the toxic effects of atropine on the cardiac vagus, blood pressure and circulation. This drug has proved to be a valuable addition to the therapy of parkinsonism and is second only to the belladonna derivatives in the extent to which it is used. In some patients who have oculogyric crises, artane causes a very gratifying improvement in this troublesome symptom.

At the commencement of treatment, three of the 2-mgs. tablets are prescribed daily. This is increased by one tablet every other day until the patient is taking 6 mgs. t.i.d., p.c. Only in the occasional case is benefit obtained from increasing this dosage. This drug is particularly welcomed by the older patients because of the low incidence of toxic side effects. It is frequently necessary after a period of artane therapy to add one of the drugs of the belladonna series as the effect of artane appears to wear off when administered alone.

The toxic symptoms encountered include dryness of the mouth, blurred vision, nausea or vomiting, dizziness or giddiness, drowsiness, tinnitus, tightness in the head, sore-

ness of the mouth, and nervousness. In a small number of patients particularly the elderly, a serious toxic encephalopathy is encountered. The patients become mentally confused, agitated, and may be dizzy with nausea. We have encountered six instances of this reaction, one of which terminated fatally. On any patient who complains of increased nervousness, a careful watch must be kept. On the whole, artane has a lower incidence of toxic side effects than the drugs of the belladonna group.

#### ANTI-HISTAMINIC AGENTS

Benadryl and thephorin have been used in the treatment of parkinsonism. In our hands, thephorin has been of no benefit. Benadryl in some cases, when added to drugs of the belladonna series or to artane, has produced an additional benefit dosage of 50 mgs. 3 to 4 i.d. The sedative effect of the drug is gratifying when the patient is tense. If benadryl is used, it should be used in conjunction with other medications.

#### AMPHETAMINE DRUGS

Both benzedrine and dexedrine are useful in the management of oculogyric crises, mild depressions, somnolence and lethargy. The usual dosage is 5 mgs. of either of the drugs, 2 or 3 i.d. If the medicine is well tolerated, it may be increased to 10 mgs., 2 or 3 i.d. Benzedrine or dexedrine taken after 4 p.m. frequently prevents sleep. Benzedrine and dexedrine are usually given in combination with other drugs directed towards relief of the tremor and rigidity of parkinsonism.

#### PARPANIT

This drug, introduced in 1946, is an antispasmodic related to "trasentine." Early reports claimed more efficiency in Parkinson's disease than that of the atropine-like drugs, but subsequent investigation has failed

to respond to any of the other medications.

The drug comes in 50 mg. tablets, and one tablet is prescribed initially with the addition of 1 tablet every second or third day until maximum therapeutic benefit. The average dose ranges between 200 to 400 mgs. per day—range from 100 to 600 mgs. per day.

The toxic effects from this drug, encountered in from 75 to 85% of the patients, are in order of frequency, giddiness, nausea and epigastric burning, feeling of lightness of the legs, and a sensation of floating.

#### TOLSEROL

(Myanesin or oranixon) Initial reports claimed favorable results following the use of this curare-like drug in the treatment of parkinsonism. Our experience has paralleled that of subsequent investigators who have found no benefit.

Toxic symptoms are rarely encountered, and include nausea, precordial discomfort, complaints of weakness either in the arms or legs accompanied by a feeling of lassitude, and pronounced increase in tremor. Two instances of leukopenia following the use of this drug have also been recorded. Early British investigators have recorded the occurrence of hematuria and hemoglobinuria but this has not been found by investigators in the United States.

#### PHYSICAL THERAPY

In patients in whom rigidity is marked, physical therapy is frequently a useful adjuvant. Mild massage, heat and directed treatments given 1 to 3 times weekly may reduce muscle soreness and relax rigidity. Regular visits to the psychiatrist afford continuity of treatment and aids in improving the patient's morale. Some of the patients benefit from speech therapy.

The purpose of speech therapy is to make the speech as intelligible as possible and to reassure the patient that it is understandable. This can be accomplished by training the patient to speak slowly and to pronounce his words as carefully as possible. If is frequently helpful to have the patient pause after each word or every phrase.

#### NEUROSURGICAL TREATMENT

There is no satisfactory surgical treatment for parkinsonism. The neurosurgical procedures currently employed are directed towards the cerebral cortex, the basal ganglia, the cerebral peduncles or the spinal cord. Only in selected cases, and this constitutes a very small minority, can the victim of this disease be helped by surgical therapy. Even in these cases surgical measures are never curative and seldom benefit more than one of the many symptoms which are present. Surgical treatment usually substitutes an undesirable neurological deficit for an even more disabling and disturbing

manifestation of the disease.

#### SUMMARY

1. Emotional rehabilitation of the patient is of prime importance if the therapeutic regime in parkinsonism is to be successful.
2. On commencing drug therapy in parkinsonism one of the following drugs is recommended: vinobel, rabellon, bellabulgara, hyoscine or artane. It may be necessary to try each of these drugs in turn or various combinations of these drugs before a satisfactory control of the patient's symptoms is obtained. Additional symptomatic relief can on occasion be obtained by the addition of benzedrine, dexedrine, Benadryl or atropine to the above medications. In the occasional patient who fails to respond to various combinations of the above medications, the use of parpanit is worth a trial.
3. Physical therapy is indicated as an adjuvant to treatment in patients in whom the rigidity is marked.



#### Effects of Regitine (C-7337)

The clinical effects of this new anti-adrenergic drug are reported in 34 patients. The pharmacologic properties of this drug are similar to those of Priscoline.

The drug was first administered intravenously and the responses were studied with temperature recordings. The drug was next given orally in doses ranging from 30 mg once a day, to 120 mg four times a day. Evaluation was largely subjective, but in many patients objective evidence was observed.

The arteriosclerotic group appeared to obtain more benefit than did the Raynaud group from the oral administration. Results in the thromboangitis group and in one patient with chronic thrombophlebitis were encouraging.

Serious side effects were few, the only reaction of any magnitude being vasomotor collapse, which occurred in two patients; minor side reactions were observed in 62 per cent of the patients.

H. D. Green, W. T. Grimsley, *Circulation*, 7:487, 1953.

## A NEW AUREOMYCIN DRESSING. RATIONALE AND USE IN THE TREATMENT OF SURFACE WOUNDS

Surface wounds, such as burns, skin graft donor sites, abrasions, excoriations, avulsions and ulcers, present special problems from the standpoint of control of infection and early closure, whenever large areas are involved. Systemic antibiotic therapy is not well suited for treatment of these conditions because effective drug concentrations are not often obtainable locally. Side reactions and cost of treatment are also important consideration in systemic therapy. Local therapy, if it can be applied effectively, has obvious advantages.

Not every antibacterial agent is suitable for local therapy. The mercurials, for example, can be used on the skin but not in wounds, because they are inactivated by serum proteins. Similarly, the sulfonamides which formerly were much used for topical application are now seldom so applied because of their sensitizing effect and interference with epithelization, especially in the case of the sodium salt sulfonamides, such as sodium sulfadiazine. Penicillin has also had considerably vogue as a topically applied antibiotic, but it, too, has disadvantages in that it is relatively unstable and subject to destruction by bacterial enzymes and otherwise.

The new antibiotic, aureomycin, makes possible a new approach to local antibacterial therapy for the following reasons: (1) the drug is substantially non-sensitizing; (2) it has a broad and safe antibacterial spectrum; (3) development of bacterial resistance to the drug is relatively uncommon; (4) it is relatively

stable in appropriate vehicles and not destroyed by bacterial enzymes; (5) it is effective in various pyogenic and other infections of the skin and thus may control dermatoses often seen at wound edges, and (6), it does not irritate or interfere with wound healing and epithelization when properly applied.

A study of 376 bacterial cultures from 77 cases, including 65 burns and 12 ulcers, before and during the course of treatment with an aureomycin dressing, demonstrated suppression of growth of pathogenic or potentially pathogenic organisms. It may be presumed that high concentration levels of aureomycin, locally obtainable from the dressing, also resulted in a suppression of certain bacteria normally classified as resistant to the drug.

No untoward reactions and no interference with wound healing were observed in the application of over 2000 aureomycin dressings on a large variety of surface wounds. Nor were there noted any contraindications for using the dressing.

It is felt that the wounds healed with unusual rapidity, as might be expected when infection is controlled and there is no chemical effect to retard epithelization. Skin graft donor sites unavoidably contaminated by adjacent burn-wounds healed with unusual rapidity under the aureomycin dressing. In brief, this dressing affords a convenient, readily available and effective means of preventing the ever-present danger of wound infection.

J. A. Tamerin, et al, *Am. J. Surg.*, 86:325, 1953.

## Factors Influencing the Reliability of a Pregnancy Test

*Histidine appears in the urine of pregnant women and its detection may be utilized as a test for pregnancy*

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R. M. CARSON and R. R. SAEKS, Dayton, Ohio

The amino acid, histidine, appears in the urine of pregnant women and its detection may be utilized as a test for pregnancy.<sup>1</sup> Several investigators<sup>2</sup> have demonstrated, however, that histidine is frequently present in the urine of non-pregnant individuals. Neuweiler and Grim<sup>3</sup> state that the amino acid can be detected in the urine of about 15% of non-pregnant women.

Normally there is but a small quantity of free amino acids excreted in the urine. The quantity increases in conditions of extensive tissue autolysis or in diseases which result in extensively impaired hepatic function.

Page<sup>4</sup> has demonstrated that pregnancy histidinuria is probably due to an inhibition or interference with the renal tubular reabsorption

mechanism for histidine. It is apparent that the renal threshold is not the same for all individuals and therefore certain controls must be established if a histidine pregnancy test is to be reliable. Factors which should be considered and which may be controlled, are as follows:—

(1) Diet. The excretion of histidine in the urine is significantly greater after a protein meal, as might be expected. It appears to reach its peak sometime before the urinary nitrogen. Therefore, a minimum of four hours should elapse between the ingestion of protein and the collection of the specimen for the test. A series of tests run on urine specimens from twelve non-

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1. Ricketts, Carson and Sacks, *Am. Jour. Ob. and Gyn.* Vol. 56, 5, Pages 955-958, 1948.

2. E. I. Plotz, *Am. Jour. Ob. and Gyn.*, Abstracts p. 471, 1943.

3. W. Neuweiler and W. Grim, *Klin. Wochschr.*, 19, 155-7, 1940.

4. E. W. Page, *Am. Jour. Ob. and Gyn.*, 51, 553-559, 1946.

From The Research Laboratory, Carson-Sacks, Inc., Dayton, Ohio.

pregnant women demonstrated that histidine could not be detected in those specimens collected four hours or more after the ingestion of protein or oral histidine. In each instance the specimens collected before the four hour elapsed period contained detectable amounts of the amino acid.

(2) Menstrual Cycle. There is an increased amount of histidine excreted in most instances, for forty-eight hours before the onset of the flow. The rate and time of increase is not the same in each individual. Following are results of tests run on specimens from twelve non-pregnant individuals:—

12 women—Positive tests throughout period of flow

10 women—Positive tests 24 hours before onset

7 women—Positive tests 48 hours before onset

The test specimen should, therefore, be collected sometime during the middle of the cycle or from one to two weeks following the first missed period. Variable results were obtained in tests made on specimens collected within a few days before or after the normal time of menstruation.

(3) Abortion. Detectable amounts of histidine are found in the urine from two to six days following abortion. The histidine excretion level then returns to normal.

(4) Specific Gravity. Urine specimens of high specific gravity collected from non-pregnant women often contained detectable amounts of histidine. By diluting these specimens with water, a histidine concentration can be established which cannot be detected by the means employed.

It is the practice of the authors to dilute all specimens of urine to the same specific gravity before testing a portion for histidine. The specific gravity of 1.008 has been chosen for alkaline specimens and 1.005 for acidic urines. The presence of 0.01125% histidine is then regarded as a positive test and pregnancy is indicated.

There are, perhaps, other factors which influence the amount of histidine excreted in the urine of non-pregnant women, but those enumerated above are most important and can be controlled. To diagnose pregnancy by testing the urine for histidine; implies a determination of an increase in the amount of amino acid excreted, and not its detection alone.



### **Piperazine in The Treatment Of Threadworms in Children**

Owing to lack of toxicity and side-effects to ease of administration, and to its excellent therapeutic properties, piperazine hydrate syrup in dosage of 50-75 mg./kg. per day is considered to be the drug of choice for oxyuriasis in children. Of 31

children treated at levels greater than 50 mg./kg. daily 97% were cured. The use of suppositories is unnecessary.

Spontaneous cure may be expected in 19% of cases of oxyuriasis.

R. H. R. White, et al, *British Medical Journal*. 4839:755, 1953.

## Infant Feeding with a Powdered Milk

*Advances in recent years have provided  
infant food formulas more nearly approaching  
the excellence of mother's milk*

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RICHARD B. TUDOR, M.D., Minneapolis, Minnesota

The perfect substitute for breast milk is too much to be hoped for. Nursing is easier, simpler, safer, healthier—better in every way than using a formula. The healthy nursing mother's milk is, with the possible exception of an adequate quantity of Vitamin C, a perfect food for her baby. When her baby is hungry and cries, his mother has only to nurse him. She need not busy herself with sterilization procedures, not worry about the correctness of the percentages. She does need to respect the prior claims of her baby on her society.

It is often necessary or desirable, however, to prescribe a formula for an infant, and then one tries to approach the quality, safety and ease of feeding breast milk. The chore of boiling bottles and nipples, measuring all ingredients including water, and adding vitamins to the average formula, can be done away with to a great extent if one uses a complete

formula food, a number of which are available.

Within recent years major advances have been made in the sciences of infant nutrition, physiology, and biochemistry. The nutritional requirements of the infant have been more clearly defined, particularly as regards amino acids, fatty acids, vitamins, and relative proportions of essential minerals. These advances have improved our concepts of infant feeding, and provided infant food formulas more nearly approaching the excellence of mother's milk.

One such formula is Bremil®, a powdered, completely modified cow's milk. The minerals have been modified by the addition of calcium, potassium and iron. The levels of calcium and phosphorus are higher in cow's milk than human milk, but cow's milk has a lower calcium-phosphorus ratio, which is an important metabolic consideration. A

number of pediatricians and investigators have discovered that the low calcium-phosphorus ratio of cow's milk is unfavorable to optimal utilization of these essential minerals, and may produce symptoms of subclinical neonatal tetany. Other symptoms of the syndrome which have been encountered are colic, vomiting, edema, and convulsions. In this formula, the calcium-phosphorus ratio has been adjusted to a minimum of  $1\frac{1}{2}$  parts calcium to 1 part phosphorus, a ratio which approaches that found in human milk. The low phosphorus content and high calcium-phosphorus ratio of this feeding make it especially suitable for the newborn infant.

Human and cow's milk normally have only minute amounts of iron. To compensate for such low levels, iron has been added to Bremil in the amount of 8 mg. per quart (reliequified). This is four times the amount found in normal human milk.

Human milk fat resembles certain vegetable fats more closely than it does cow's-milk fat. By replacing butterfat with a specially selected blend of vegetable oils, the fatty-acid pattern of the product under discussion very closely follows that of human milk. This change in the fat content appears to be mainly responsible for its quick and easy digestibility.

It has been shown that casein and lactalbumin are approximately equivalent for human nutrition, although casein is somewhat deficient in sulfur-containing amino acids, e.g., methionine, and in tryptophan. The addition of methionine corrects this deficiency, and when supplied at an adequate level tends to prevent the formation of ammoniacal urine.

The metabolism of tryptophan and that of the B vitamin, niacin, are interrelated. Thus, when provided in adequate quantity, niacin spares the

tryptophan for its important role as one of the essential amino acids and prevents its utilization for synthesis of niacin by the body. Both tryptophan and niacin are necessary for growth, and both have been adequately taken into account in this formula. In short, the percentages of the essential amino acids have been adjusted so as to constitute a pattern conforming closely to that of human milk, as shown in Table I.

Vitamins A, D, C and the B vitamins (thiamine, riboflavin, and niacin) have been added to provide the infant with his daily requirement of these important nutritional factors, as established by the Food and Nutrition Board of the National Research Council. Although I have not seen any cases of rickets and scurvy since I have been using this infant food—well over two years now—I felt that a larger margin of safety could have been assured by the addition of more ascorbic acid. This has now been done to provide 50 mg. per quart (reliequified).

These several hundred babies gained weight better than those on other formulas, and did practically as well in every way as those on breast milk.

I introduce this formula to my patients by suggesting:

- (1) that it is the simplest cow's milk formula to prepare
- (2) that it is well-nigh impossible to make any errors in preparing the formula, as there is nothing for the mother to add but water.
- (3) that the mother doesn't have to use hot water or even boiled water in the preparation of the formula. If she wants to use boiled water, this can be prepared hours before the formula is required.
- (4) that because of its easy and rapid solubility in cold water, one bottle can be made up in

Argin  
Histic  
Lysin  
Trypt  
Phen  
Cysti  
Threo  
Leuci  
Valin

(5)

(6)

Adm

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**TABLE I**  
**Amino Acid Patterns**

	Human Milk gm./qt.	Formula gm./qt.
Arginine	0.53	0.54
Histidine	0.36	0.32
Lysine	0.92	1.08
Tryptophan	0.21	0.20
Phenylalanine	0.70	0.80
Cystine & Methionine	0.50	0.72
Threonine	0.60	0.67
Leucine & Isoleucine	2.29	2.75
Valine	1.16	1.04

a few seconds, after the baby starts to cry from hunger. The mother can therefore omit the usual chore of making up six or eight bottles of formula ahead of time. She waits until the baby cries, then pours the required amount of cooled water in the bottle, adds the powder, shakes the bottle a few times, and offers it to the child

- (5) that it is safe in every way for the baby
- (6) that this food cost no more than other foods when full consideration is given to its completeness.

#### SUMMARY

- (1) The formula described, a powdered modified cow's milk for infants, is suggested as an excellent food for infants and babies that are, for any reason, denied breast milk.
- (2) Its satisfactory use for two years in feeding over 200 infants is described.
- (3) It is suggested that the use of this formula will save the average mother much time in the preparation of the baby's formula.

Bremil®, a product of The Prescription Products Division, The Borden Company, New York.



#### Administering Dicoumarol

Recommendation is made that dicoumarol be administered continuously, that is, by daily maintenance dose rather than by intermittent doses. A single initial dose of 250 mg. followed by 125 mg. on the following day is advocated at the beginning of treatment in all cases, the dosage being regulated there-

after by estimation of the prothrombin time or prothrombin index (by Öwren's one-stage method) thrice weekly, attention being paid to the trend of the curve rather than to the actual prothrombin level on any one occasion.

C. J. Bierkelund, *Lancet*, 1:260, 1953.

# The Treatment of Acute Respiratory Infections

CHRISTOPHER PARNALL, JR., Rochester, New York

For the common cold most patients want something done. If your patient likes liquor, a hot toddy or two; otherwise, aspirin and penacetin. Cough syrups with codeine in them are most effective.

A fever of 100° and raised w.b.c. count may mean a bacterial infection. Start with a sulfonamide, it is cheap and can be taken by mouth. If improved in 24 h., well and good; if not, penicillin should be added—and don't forget to ask your patient whether or not he is sensitive to these drugs before giving them. If he is not better, in another 24 h., if white count be normal or low, a virus is more likely to be the infecting agent. Wait a short time, particularly if there is an increase in the lymphocytes.

A patient only moderately ill with a t. of 102°, a 24-h. trial of antibacterial treatment may be carried out in the home; if there is no improvement send him to hospital and have blood and sputum cultures, white count (with diff.) examined if count is high and mainly neutrophils, a sulfonamide or penicillin, or both, are indicated. If the count and differential are normal, or with an in-

crease in lymphocytes, try aureomycin or terramycin. According to the results of cultures, treatment is guided by the type of organism found and its sensitivity to the various antibacterial agents.

Accurate detection of the viral and rickettsial pneumonias requires equipment so extensive and expensive, and is so time-consuming, that it is in general neither practicable nor possible. Occasionally, the history of contact with birds or the skinning of cattle will give a clue to possible psittacosis or Q-fever. Otherwise one can only judge from the clinical picture and the white blood count and act accordingly.

A patient with definite pneumonia "crackles" in his chest, or a positive chest x-ray film or both, given treatment, promptly gets well at home or in hospital. Have a chest film taken at the time that he is apparently well to make sure that his lungs are completely clear. If you do not do this, you will miss an occasional case of tuberculosis and an occasional case of cancer of the lung. Always follow a patient with lung disease with the x-ray film until it is clear.

*Jour. La. State Med. Soc.*, 105:375, 1953.

## Treatment of The Nipples in Preparation of Breast Feeding

*Extreme engorgement can be prevented  
by starting manual expression of colostrum from the  
breasts three months antepartum*

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FRANK HOWARD RICHARDSON, M.D., F.A.C.P., F.A.A.P.,  
Asheville, North Carolina

Most cases of premature weaning are due to insufficiency of milk secretion and pain and damage to the nipples. Since painful nipples are so often the cause of insufficient milk secretion, because a mother suffering pain does not permit her baby to give the stimulation necessary to maintain the flow, it is safe to assert that sound nipples are almost essential to successful breast feeding.

But how are the nipples to be saved? What is the best course to pursue in order to conserve this essential link in the chain of breast feeding? The methods used have varied widely and have been dictated by varied theories. One obstetrician<sup>1</sup> states the case as follows:

"Among the methods recommended by various authorities are the

use of alternating hot and cold water, brushing the nipples, the use of alcohol to harden them, ointments to soften them, massage with bare fingers or rubbing with everything from super-fatted soap, lanolin, and cologne water to cocoa butter, olive oil, etc. The best toughener for the nipple however is a nursing baby."

These various methods of "conditioning" the nipples have been predicated upon the idea that the skin covering the nipples is an inert, inactive, protective membrane, which must be made resistant by being toughened, according to one school of thought, or kept pliable and soft, yet resistant, according to those who favor the opposite plan. Both methods agree on one point, namely, that the skin must be rendered as nearly sterile as possible. Hence, abundant washing with soap and

<sup>1</sup> Howard C. Walser, *Psych. Med.* 7:174, 1945.

water, followed by some sort of bacteria-inhibiting application, has been the order of the day.

Niles Newton, a careful investigator in the field of lactation, suggests an entirely different thesis however. She insists that the body has mechanisms for protecting the skin of the nipples and inhibiting bacterial growth and that most of the methods used to strengthen them actually weaken them by interfering with these mechanisms. She therefore proposes an unusual but most sensible-sounding regimen, growing out of her practical studies in the Jefferson Hospital, Philadelphia. Newton strongly opposes the use of soap, since it removes the epithelial cells on the surface that protect the nipples. She is equally opposed to the use of alcohol, which, while hardening the skin abstracts the water and precipitates the protein it contains. Hence, it leaves the skin more liable to fissure, rather than less vulnerable to injury from the baby's nursing. She also points out that the skin of the nipples is more abundantly supplied with sweat and sebaceous glands than any other part of the body and that they increase in activity prenatally. Soap and water, alcohol, and almost any other of the agents popularly employed, naturally lessen the power of the nipples to resist both infection and the vigorous action of the nursing infant. She lets mothers expose the nipples to the air as much as possible and finds that except in cases of extreme pain, shortening or stopping the baby's nursing is not necessary, since his normal nursing does not retard the healing of moderately damaged nipples.

None of these methods of conserving the integrity of the skin of the nipple, however, deal specifically with a phenomenon with which everyone who observes nursing

babies should be familiar. It has been termed "engorgement" and poses the greatest hazard to the continuance of nursing. It has been studied more intensively by Waller than by any other observer.<sup>2</sup> He analyzes the whole business of the mechanism of the baby's way of getting the milk that is not generally recognized.

Walter believes that the child's role in nursing is, by no means, mainly fulfilled by suction. He believes that suction draws the nipple far back into the nursling's mouth, and holds it there while he forces his lower jaw up against the roof of his mouth and squeezes the ampullae in a rhythmic action.

The active milk secretion, beginning a few days following labor, replaces the colostrum that the breasts have been secreting for several months antepartum. In about a fifth of the total number of mothers, this change is not too uncomfortable. The filling up with true milk is marked by moderate breast enlargement or tension; and what tension there is, is relieved by a slight leakage of milk. This soon adjusts itself to the demands of the baby, who empties the breast quite successfully within a few days.

Perhaps another one fifth are those mothers who suffer, and may suffer intensely, from true "engorgement;" the "coming in of the milk" is extremely disagreeable and painful for them. The breast becomes very hard, swollen, even edematous from the oversupply of milk, and there is no leakage to relieve the distention. In this situation the nipple is hard, and not at all flexible in its attachment to the breast.

As a result, the baby cannot get hold of the portion of the breast underlying the areola where the milk

2. Harold Waller, *Arch. Dis. Childhood* 21:1, 1946.

reservoir lies, which he must compress with his lower jaw against his palate if he is to get any milk. All he can do is mouth the nipple, chew on it and bite it, with consequent serious damage and extreme pain to his mother. He gives her no relief by this incessant painful sucking because he cannot withdraw any milk. Meanwhile, the pressure inside the breast tends to diminish milk secretion so that this engorgement is frequently the cause of a permanent drying up of the breast, and consequent premature undesired weaning.

The remaining three fifths of nursing mothers vary between two extremes; at one end of the spectrum, little or no discomfort is experienced and satisfactory nursing is established within a few days. Pain and tension in the breast so severe that nursing is terminated quickly, perhaps with the formation of actual breast abscess, is experienced by mothers at the other end of the spectrum. How shall these various degrees of engorgement be treated?

Obviously, little needs to be done for those near the lower end of the scale. But for those with extreme degrees of engorgement, prompt action must be taken to avert serious complications. Elevation, attempts to remove some of the milk by manual expression or by breast pump, hydrotherapy, even small doses of stilbestrol, may or may not help; while the tender nipples continue to be mouthed and chewed by the infant in his utterly unproductive attempts to get out the milk.

This condition is so difficult to treat and so comparatively easy to prevent, that the means of forestalling it should be considered seriously in the case of subsequent pregnancies of any woman who has

once suffered from engorgement in its severer forms.

Prevention<sup>3</sup> can be brought about by starting the manual expression of colostrum from the breasts as early as three months antepartum. The patient is instructed to grasp that portion of the breast just back of the areola (or pigmented area at the base of the nipple), between the thumb and forefinger of the opposite hand. She brings these together with a pinching motion that compresses the milk reservoir and forces out the colostrum, just as the milk will be forced out after the baby has arrived and is nursing. This manipulation will force a thick, sticky yellowish fluid to exude from the little duct openings on top of the nipple.

If the colostrum comes out easily and readily, with no indication of any blocking at the mouths of the ducts, it is not necessary to do this oftener than every other day, or even only twice a week if the flow is very free. If it does not come readily, the manipulation had better be performed daily. Those who have had experience with this method say that it gives an extra dividend in the form of easier establishment of lactation generally, in addition to doing away with severe engorgement.

Readers may be disappointed that no hard and fast method of safeguarding the nipples, the essential factors in successful breast feeding has been presented and that instead, several suggestions have been offered, some of them seemingly contradictory. The answer to this objection is obvious--this highly important business of nipple conservation is still in the twilight zone of undetermined practise. Like so

3. Editorial, *J.A.M.A.*, 132:151, 1946.

many other things in the practice of medicine, this problem is something that calls for careful study, controlled by unprejudiced observation of parallel groups subjected to various regimens. The greatly renewed interest in breast feeding will

certainly solve the problem before long. This interim can be shortened if observers will report their findings impartially, so that a fund of experience can be built up on which sound conclusions may be based.



### **Gastric Function in a "Decorticate" Man with Gastric Fistula**

This study appears to confirm the contention that variability in gastric function depends in part on situations which have special significance for the individual.

Measurements were made of gastric function in a 30-year old unconscious man with a gastric fistula five months after a head injury. His neurologic status closely resembled that of a decorticate preparation. This patient displayed a basal gastric secretion and motor activity which fluctuated in rhythmic fashion within wide limits throughout the 24-hour period. It was possible to modify this spontaneous cycle by the ingestion of food or the administration of certain pharmacologic agents, but not by noxious stimulation. Although parasympathomimetic agents induced gastric hyperfunction, there was no response to repeated intravenous injections of insulin in amounts adequate to produce hypoglycemia. The absence of

insulin response has been confirmed in another "decorticate" man.

It is well known that small doses of atropine produce variable and unpredictable responses in intact individuals. This has been thought to be due to modification of the atropine effect by other influences acting on the end organ at the same time, including life situations. The response to atropine in this man, who was unable to interpret events around him, was monotonous and readily reproducible. This finding, coupled with the absence of changes in gastric function during noxious stimulation, is in keeping with inferences drawn from the study of fistulous individuals with intact higher neural centers. It would appear to be confirmed, therefore, that variability in gastric function depends in part on situations of special significance for the individual.

R. K. Koig, et al, *Clin. Research Proc.*, 1: 46, 1953.

## Acute Intussusception in Adults

*Because of the lack of uniformity of clinical symptoms in adolescents and adults a correct preoperative diagnosis is rare*

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WALTER F. BECKER, M.D., F.A.C.S., New Orleans, Louisiana

While intussusception is one of the most common causes of obstruction encountered by the English surgeon, in most American clinics it is responsible for less than 10 per cent of such cases. Infants and children under 2 years of age account for about  $\frac{3}{4}$  of the patients with acute intussusception, and it is the typical clinical picture presented by the disease in this age group with which most physicians are best acquainted.

That this variety of obstruction occurs in adults and adolescents with such frequency as to warrant consideration is suggested by a recent review<sup>1</sup> of 1007 cases of acute mechanical obstruction occurring consecutively at the Charity Hospital in New Orleans during the 10-year period 1940 to 1949. Eight per cent of the cases of acute intussusception seen at this institution during this period occurred in patients

14 years of age or older. Four additional adult cases were observed in 1951. The purpose of this report is to briefly discuss these 10 cases of adult intussusception, and to re-emphasize some of the important differences between the adult and infantile forms of the disease.

Intussusception is ileocecal in 60 per cent of the cases, ileocolic in 30 per cent, and the remaining 10 per cent are of the enteric and colic varieties. Thus the majority of intussusceptions in infants and young children occur about the ileocecal region. While most reports indicate that the colon is the most common site in the adult, only 1 of the 10 cases in the Charity Hospital series was of the colic variety. Five were enteric, 3 were ileocecal, and 1 was ileocolic.

In most cases of intussusception observed in infancy it is impossible

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1. Becker, Walter F., *Intestinal Obstruction* (In press).

to identify a definite etiologic factor, whereas in adults the invagination is usually initiated by the drag of a pedunculated neoplasm, Meckel's diverticulum, ulceration, etc. A study of 300 cases of adult intussusception by Eliot and Corscaden<sup>4</sup> disclosed a neoplasm present in 40 per cent, 24 per cent benign and 16 per cent malignant. Tuberculous, bacillary, or typhoidal ulceration in the bowel was present in 14 per cent of the cases, a Meckel's diverticulum in 12 per cent, and in a few instances these authors believed that trauma had initiated the invagination. In the Charity Hospital series of 10 cases<sup>3</sup> a tumor was found at the apex of the intussusception in 8 cases, a tuberculous ileal ulcer was the presumptive etiologic factor in 1 case, and the other 2 cases were "idiopathic."

About 75 per cent of all acute intussusceptions occur in infants and children before the end of the first two years of life, and in this age group the clinical picture is usually so characteristic that diagnosis is easy. Almost invariably present are the 4 cardinal symptoms of the disease:

1. Periodic attacks of pain
2. Vomiting
3. Passage of blood and mucus by rectum
4. Presence of a palpable tumor in the abdomen.

This uniformity of the clinical picture is lacking in adults. While vomiting and cramping abdominal pain were experienced by every patient, blood was passed by rectum or was detected by digital examination in only 3 of the 10 cases, and a mass was palpable by abdominal or rectal examination in only 4 cases. Five of the patients had diarrhea.

It is interesting that recurrent intussusception in infants and young children appears to be rare; but

adults with intussusception usually tell of repeated attacks of abdominal cramps, vomiting and other obstructive symptoms. Eight of the 10 patients in the present series had experienced similar, less severe attacks.

Because of the striking uniformity of the clinical picture presented by the infant and young child with acute intussusception, a correct pre-operative diagnosis can almost invariably be made, or at least strongly suspected. Acute adult intussusception is rarely diagnosed before operation.

#### OPERATIVE REDUCTION

Early operative reduction of the invagination is the preferred treatment. The writer feels that this is a therapeutic principle to which the pediatrician and surgeon should adhere, though he is aware of the fact that intussusception has been reduced by hydrostatic pressure with barium enema with remarkable success in certain clinics.<sup>5, 6</sup> Non-operative reduction probably should not be attempted in adults, because of the frequency of intestinal neoplasms exist as the causative factor.

The surgical maneuver employed in the individual case of acute adult intussusception must vary with the site, etiology and reducibility of the invagination; the presence or absence of strangulation; and the general condition of the patient. In the early stages, reduction can usually be easily accomplished without permanent damage to the bowel; and simple reduction is all that is required in instances of reducible, non-strangulated, idiopathic intussusception. When the interval between the onset of the invagination and the time seen by the doctor has been prolonged, edema, adhesions and

2. Becker, Walter F., *Surg. Gyn. Obst.*, 96:677-682, 1953.

3. Becker, Walter F., *J. Louisiana State Med. Soc.*, 105:110, 1952.

4. Eliot, E., Jr., Corscaden, J. A., *Ann. Surg.* 53:169, 1911.

gangrene may have made reduction impossible and resection mandatory. Irreducibility, strangulation and the presence of a neoplasm as the etiologic factor are three indications for resection; but the time of the resection and its exact method of execution will be decided by many factors. For example, enteric intussusception on the basis of a single pedunculated polyp, whether of the simple, strangulated, reducible or irreducible variety, is usually managed by resection and immediate restoration of intestinal continuity. On the other hand, it is easy to conceive of a rare set of circumstances under which the surgeon may consider it wiser to treat even the patient with enteric intussusception by simple exteriorization of the involved bowel in a Mikulicz fashion, with closure of the enterostomy at a later date.

Acute adult colo-colonic intussusception is usually a much more complicated problem to which a somewhat different set of therapeutic principles must be applied. One of the major factors responsible for the continued high mortality of acute mechanical intestinal obstruction is failure to appreciate the many differences between large and small bowel obstructions.

#### COLON RESECTION

Colon resection in the presence of acute obstruction is dangerous. A recent review<sup>2</sup> of 205 cases of acute complete large bowel obstruction seen at Charity Hospital shows that 21 patients were treated by immediate resection with a mortality rate of 62 per cent. Immediate resection of an acutely obstructing carcinoma was performed 10 times with 7 deaths. This mortality of 70 per cent is to be contrasted with one of 8 per cent in patients with acutely obstructing colon carcinoma who survived a primary surgical decom-

pression and later had elective resection.

#### CARCINOMA

A carcinoma is responsible for most cases of acute colic intussusception occurring in adults. Reduction of the intussusception and proximal surgical decompression, followed in a few days by elective resection, is the preferred method of treatment. Unfortunately, in many cases this plan cannot be followed because of the existence of irreducibility or strangulation. Under these circumstances resection with delayed anastomosis employing the Mikulicz principle is a useful procedure. Simple proximal decompression under local anesthesia will occasionally be justified in the gravely ill patient who 24 to 48 hours later may be able to tolerate exteriorization or exteriorization-resection of a gangrenous irreducible colic intussusception.

#### PREOPERATIVE PREPARATION

Preoperative preparation of the patient by suction applied to a long intestinal decompression tube and the correction of fluid, electrolyte and blood volume deficits is of great importance, but it must not be permitted to delay the operative attack.

#### SUMMARY AND CONCLUSIONS

Only 10 per cent of patients with acute intussusception are over 14 years of age.

Ten cases of adolescent and adult intussusception are reported with two deaths.

In infants and young children the signs and symptoms are usually so characteristic that diagnosis is simple; but this uniformity of the clinical picture is lacking in adults and adolescents, and in this latter group a correct preoperative diagnosis is rarely made.

5. Hipsley, P. L., *M. J. Australia*, 2:201, 1921.

6. Ravitch, M. M., Morgan, R. H., *Ann. Surg.* 135:596, 1952.

# Clinical Evaluation of Pro-Banthine\*

## CASE REPORT

"M. D., female, aged 48, had a posterior gastrojejunostomy 14 years ago for duodenal ulcer. The patient was fairly well until nine months ago when severe, intractable pains occurred. She was hospitalized and a subtotal gastrectomy was done.

"She remained well for only a few months and was referred to us because of recurrence of very severe pain and marked

\*Trademark of G. D. Searle & Co.



Fig. 1: "Roentgen examination... revealed the ulcer to be very much in evidence."



Fig. 2: In ten weeks "the ulcer niche was no longer in evidence roentgenologically or gastroscopically."

weight loss. Roentgen study revealed a fairly large ulcer niche on the gastric side of the anastomosis.

"The patient had been on various types of antacids and sedatives without relief from pain. She was given 60 mg. of Pro-Banthine q.i.d. and within 72 hours was able to sleep through the night for the first time in weeks.

"At the end of two weeks of such treatment the patient had absolutely no pain and felt that she had been 'cured.' Roentgen examination at this time revealed the ulcer to be very much in evidence (Fig. 1). Much persuasion was necessary to make the patient realize the importance of maintaining her diet and therapy.

"Ten weeks of controlled regulation was necessary before we were satisfied that the ulcer niche was no longer in evidence roentgenologically or gastroscopically (Fig. 2).

"She has been maintained on 30 mg. of Pro-Banthine for almost five months with no recurrence of symptoms."

Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, to be published.

Pro-Banthine (*brand of propantheline bromide*), the new, improved anticholinergic agent, is more potent and, consequently, a smaller dosage is required and side effects are greatly reduced or absent.

Peptic ulcer, gastritis, intestinal hypermotility, pancreatitis, genitourinary spasm and hyperhidrosis respond effectively to Pro-Banthine, orally, combined with dietary regulation and mental relaxation.

SEARLE Research in the Service of Medicine

## INTRANASAL MEDICATION WITH AN ANTIBIOTIC-DECONGESTANT SOLUTION

Decongestant nose drops are indicated in simple catarrhal, hypertrophic and hyperplastic rhinitis, and the nasal complications of acute or subacute upper respiratory tract infections of bacterial origin, especially those with paranasal sinus involvement.

A properly constructed solution contains a vasoconstrictor, an antibiotic and an anti-histamine without untoward side reactions.

Biomydrin (*Nepera*) is composed of Neomycin sulfate, 0.1%; Gramicidin, 0.005%; Thonzylamine HCl, 1.0%; Thonzonium bromide, 0.05%; Thonzylamine HCl, 1.0%; Thonzonium bromide, 0.5%; Phenylephrine HCl, 0.25%, and is packaged in a disposable plastic "squeeze bottle" capable of delivering a fine spray, or in plain bottles for use with a dropper or power atomizer.

Neomycin is stable, has a broad range of antibiotic activity, is effective over a wide range of pH, is not affected by body fluids and does not readily lead to sensitization or resistance. Gramicidin is specific for gram-positive organisms and has been used topically for many years with practically no side effects. Neomycin is used systematically only rarely, and gramicidin, never; thus the possibility of sensitizing the patient to antibiotics which might later be essential for systemic use, and the development of resistant strains of micro-organisms are virtually precluded. Thonzonium bromide, in addition to its mucolytic properties, has potent bacteriostatic and bactericidal effect on gram-positive organisms. It potentiates the antibiotic activity of neomycin and/or gramicidin on gram-positive organisms in a truly synergistic manner. The value of antihistamines in allergic rhinitis and in acute or chronic respiratory tract infections is established; hence

inclusion of the antihistamine, thonzylamine hydrochloride, an effective antihistamine with virtual freedom from side effects. The vasoconstrictor, phenylephrine hydrochloride is widely used, has a rapid and lasting effect and an almost complete freedom from side reactions.

Unselected patients with infections of the upper respiratory tract, with nasal or paranasal sinus involvement, were studied clinically and bacteriologically, the majority during the winter of 1952-53. Cultures on 97 if these patients were taken from the nasal passages before treatment and inoculated, the organisms identified by the usual bacteriologic technics. The patients were given one week's supply of the medication and instructed to spray two or three times into each nostril according to need up to five or six times a day. Children were given one to two sprays, four to five times a day. When drops were used instead of the spray, the patients were instructed to instill five drops into each nostril —?— 4 h. The spray was soon found to be preferable, so has been used almost exclusively. The patients were reexamined within two days after medication was completed and repeat cultures were taken at this time whenever possible.

A total of 124 patients has been studied to date in this manner. Complaints—stinging sensations, nausea, excessive drying, etc.—were rare. Most of the patients found at least partial relief of their symptoms within a few minutes after medication.

This antibiotic decongestant solution has been found to be of great value from the standpoint of effectiveness, safety and patient's acceptability.

Lazar, A. M., Goldin, M., *Eye, Ear, Nose & Throat Monthly*, 32:512-515, 1953.

# The Management of Cirrhosis of the Liver

*In patients suffering from  
Laennec's cirrhosis, the control of  
alcoholism is the basic problem*

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JOSEPH POST, *New York*

Laennec's cirrhosis of the liver is the term used herein to define that complex of clinical, functional and anatomic sequelae which occur in this part of the world, most frequently associated with chronic alcoholism. There is another type which follows viral hepatitis, which is becoming increasingly common.

Laennec's cirrhosis may present as an occult disease, diagnosed by liver biopsy, operation or at post-mortem. Sometimes there is malnutrition, weight loss, peripheral neuritis, and/or glossitis, a palpable liver, "spider" angiomata, "liver" palms, and/or a palpable spleen.

A nutritious diet (carbohydrate 350, protein 100, fat 125) is the basic treatment. Vitamins of the B complex are given if there is evidence of specific vitamin deficiency states

or if alimentation is poor. Their parenteral use may be necessary. Usually, considerable guile is needed to obtain adequate patient cooperation. When this has been accomplished, the therapeutic results are most gratifying. Control of alcoholism in these patients becomes the basic problem.

This cirrhosis present as a severe and progressive disease with wasting, ascites, edema, and icterus, anorexia and abdominal pain, difficulty in maintaining nutritional intake. Where a diet such as indicated cannot be ingested, we have employed a drink containing 1 quart of milk, 4 to 6 raw eggs, 4 tablespoonfuls of lactose, and 5 to 10 tablespoonfuls of a protein hydrolysate, flavored to the patient's taste. This will meet the patient's basic caloric needs in a

concentrated form. Additional food may be given as tolerated. The use of 6 to 8 small feedings per day is helpful. Great care may be necessary to make the food attractive. For those patients who can eat nothing, such as those in coma, intravenous glucose (20% in distilled water, 2 L. per day) with added water-soluble vitamins and IV salt-poor human albumin may be given.

Ascites and edema complicate the situation. The abdominal distention causes discomfort and interferes with food intake, and paracentesis for relief of distention also removes valuable protein and electrolytes. Our policy has been to drain the abdominal cavity for the patient's comfort in order to help him eat.

The measures employed to control fluid retention are: (1) mercurial injections with or without ammonium chloride reinforcement, (2) sodium-restricted diets, and (3) exchange resins.

The mercurials may be given twice weekly with ammonium chloride (3 to 5 Gm.) daily for reinforcement. A diuretic response to

mercurials is a good prognostic sign. Often these responses are not favorable. Since large amounts of potassium may be lost, whether or not sodium and water are lost, it is well to check for hypopotassemia in such patients and to replace potassium where needed. Since it is more important for the patient to eat well of nutritious food than to restrict his salt intake rigorously, a useful tool in such cases is the ammonium-potassium exchange resin. This compound takes up sodium from the bowel. When used with care, it can be of considerable help, it may obviate rigid salt restriction, and it may be used along with mercurials.

In a recent series of 28 patients, seen during the first episode of ascites and edema, 24 patients improved with diuresis within the first two months of hospitalization. Continued well-being may be expected after diuresis, provided the patient continues to eat well, to abstain from alcohol, and provided he does not suffer the rupture of an esophageal varix.

*New York State Jour. of Med.* 53:16, 1953.

### **Corticotropin And Adrenal Hormones During Operative Stress In Endocrine Disease**

Patients with pituitary or adrenal deficiency do not tolerate surgery well because of inadequate protection against stress and attending protein depletion. Such patients should be kept for several days prior to surgery on a diet rich in calories and protein, supplemented with hormone therapy, in particular, corticotropin and testosterone. If corti-

cotropin does not provide adequate adrenal stimulation, or if immediate surgery is necessary, cortisone and adrenal extract should be given in large amounts during and after operation. The case histories of three patients with pituitary deficiency are cited to illustrate the procedure.

L. H. Kyle, et al, *A.M.A. Arch. Int. Med.*, 91:283, 1953.

## Interpretation of Functional Versus Organic Murmurs by Cardiodynamic Methods

*It is apparent that functional systolic murmurs, from a vibrational standpoint, differ from organic murmurs*

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From the standpoint of accuracy probably the best way to hear a sound originating in the chest wall is by pressing the ear tightly against the chest wall. The soft skin and flexibility of the ear make an airtight contact, and the volume of air included is small enough so that resonance and echoes are at such a high pitch that they do not interfere. Laennec's one-ear, rigid stethoscope transmitted sounds well, since the air volume was still small and accurately contained, although it was more difficult to keep this system airtight. The binaural stethoscope introduced a much greater air volume and, in addition, variable lengths of rubber tubing and chest pieces and ear pieces of various irregular shapes. The net result was an instrument which had about all the possible acoustic errors. The flexible stethoscope results in re-

sonance or reenforcement of certain frequencies while a nearby frequency may be almost completely lost, e.g. a frequency of 200 cycles per second may be transmitted several hundred times better than one of 100 cycles.

There is another important difficulty in listening to heart sounds. A large portion of the energy transmitted to the precordium is in the form of low-frequency vibrations at the lower limits of hearing. At the high-frequency limit the sensation of hearing simply disappears; at the low-frequency limit perception persists but is variously distorted.

All this has much to do with the problem of differentiating murmurs. We have avoided the stethoscope and tubing and the use of the ear as a detecting device, and have approached the problem from the standpoint of vibrational analysis.

The microphone is calibrated in dynes—units of force—and the sensitive element of the microphone is in direct contact with the precordium thus avoiding the resonance and harmonic problems of the flexible stethoscope. We record the heart vibrations from the precordium photographically and, since the recording system can be adjusted to within 5% error, it is possible to study the location, direction of transmission and attenuation of sounds, or time their appearance in various areas of the precordium.

In our present series of 20 cases of functional systolic murmurs it is apparent that, from a vibrational standpoint, they differ from organic murmurs in that: (1) they have a nearly pure frequency of 90 to 130 cycles per second; (2) the systolic

murmur does not interfere with the first heart vibration and stops definitely before the second heart vibration begins; and (3) there is a characteristic distribution along the left border of the heart extending up into the base of the heart. To date none of such murmurs has been found to be organic.

Organic murmurs have a variety of frequencies, can invade or replace the first vibration, can extend into or through the second vibration. They can be of an inaudibly low frequency such as are found in some instances of patent foramen ovals or defects in the interauricular septum. The shunt character of a murmur is much more easily analyzed by the vibration technique than by stethoscope or phonocardiography.

*Nebraska State Med. Jour.*, 38:296, 1953.



### Intravenous Gitalin

Sixteen patients with congestive heart failure and 4 healthy subjects were given doses of gitalin (a combination of the aglycone gitaligenin with 2 molecules of digitoxose) intravenously and studied with respects to the effects produced. For comparison strophanthin K, lanatoside C, and digotoxin were also used.

An initial dose of 2.5 to 3 mg. of gitalin was well tolerated, and full digitalization was obtained by two injections at an interval of 24 hours. The effective maintenance dose was found to be 2.5 mg. twice weekly. There were no side effects, such as nausea and vomiting, which would confirm the claim that the therapeutic ratio is higher than with other glycosides. Of the 16 patients treated, two had failed previously to respond to other digitalis prepara-

tions and had shown reactions to them; they responded well to the new drug and gave no evidence of side effects.

It is concluded that the wide margin of safety of the drug and the relative lack of side effects seem to indicate gitalin as the drug of choice in patients with congestive heart failure due to rheumatic carditis or coronary disease, and in patients with cardiac failure exhibiting evidence of hyperexcitability of the myocardium (ectopic rhythms). On the other hand, ambulatory patients on maintenance doses of gitalin should be checked at frequent intervals because the rapid elimination of the drug may lower the blood level of digitalis below the effective figures.

O. M. Haring, et al, *Am. Heart J.*, 45:108, 1953.

## Office Gynecology

*The need for a periodic check-up examination for the older woman cannot be overemphasized*

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JOHN PARKS, M.D., Washington, D. C.

The physician's office is where most gynecologic diagnoses are made, and it is where those few patients who need hospitalization are usually informed of their pathologic conditions. A patient with a gynecologic problem reports to her physician because of: Fear, pain, abnormal bleeding, leukorrhea, tumor mass, or marital difficulties. Often the patient shows reluctance to relate the real reason for her visit, particularly when she fears cancer or when her problem is that of sexual maladjustment.

Following a full account of symptoms, a general examination is completed by investigation of the pelvic structures. The five essentials of pelvic examination are:

1. Position: relaxed lithotomy or Sim's position.
2. Illumination: adequate light is a necessity.
3. Inspection: look before palpating; see the cervix.

4. Palpation: bimanual vaginal-abdominal; rectovaginal-abdominal.

5. Cogitation: think over all the evidence.

It is easier to understand symptoms and interpret physical findings when they are related to the five periods of feminine life.

### PERIOD OF INFANCY AND CHILDHOOD

*The Newborn.* Sex differentiation is usually very easy but is always a real responsibility. When in doubt about the sex of a new baby, seek consultation. Never operate at any time on such a patient until all physical and emotional aspects have received complete consideration. Genital spotting of blood in the newborn is usually transitory and of no significance. If bleeding persists look for a genital tumor.

*Childhood.* Gynecologic symptoms in children usually consist of leukorrhea, of bleeding, or of a tumor. Leukorrhea may be due to vulvova-

ginitis, urethritis, or proctitis. Gonorrhea is rarely encountered. Much more frequently genital discharge from a child is due to a foreign body, to trichomonas vaginalis, to pinworms, to malnutrition, or to masturbation. Pelvic tumors in children are uncommon. Genital bleeding may be of traumatic or of endocrine origin.

With the little girl on her side facing away from the physician, rectal abdominal examination can be performed, usually with ease by using a small finger. To take a smear or visualize the vagina, the child's upper leg should be flexed and the examination completed with an otoscope or a small nasal speculum at body temperature.

#### PERIOD OF ADOLESCENCE

The pubescent girl is often presented to her physician because of unusual growth or abnormal menses. It is usually wise to take a history from the mother followed later by a talk with the girl alone. Emotional balance between mother and daughter, diet and assurance help the majority of these patients. Unless there is absolute evidence of hypothyroidism, thyroid medication is contraindicated.

An erratic beginning is as likely as an irregular ending of menstruation. If after complete examination, there is no apparent cause for the bleeding, menorrhagia is best treated by observation, assurance, rest, and occasionally by the cyclic use of estrogen or progesterone. Delayed onset of menstruation may be normal up to the age of 17 or 18 years. It is important not to darken the patient's mental outlook with a diagnosis of "infantile womb." Given time the uterus usually develops to proper proportion and functions properly. Patients who experience premenstrual swelling and pain with the on-

set of the period are often benefited by sodium restriction and ammonium chloride during the week before menstruation. For many of these young patients it is best to perform any pelvic examination in the hospital with the aid of a short acting general anesthetic.

#### THE REPRODUCTIVE PERIOD

Whether married or unmarried, the majority of mature women who report to your office want advice about their reproductive systems. If a young couple ask for examinations and suggestions prior to marriage, a tactful evaluation of the couples' knowledge of anatomy and reproductive function and a complete physical examination are in order. Major concern often centers about the hymen. Significant constriction is an indication for gentle dilation of the hymen. Hymenal dilation is less traumatic than hymenotomy. These young people should be sent forth from the office with knowledge of the normal female anatomy and with a healthy confidence in themselves.

There is a growing trend among informed women to report at intervals for physical examination. This is a real safeguard to health. Some physicians even set aside special office time for the examination of their healthy patients and remind those who procrastinate in returning for their check-up examinations.

Major among feminine fears are: cancer, pregnancy, infertility, and a feeling of being abnormal. Following any pelvic examination or laboratory study, the patient experiences a sense of relief in being told that she has no evidence of cancer or that her genital organs are normal. Fears of pregnancy may be removed by proper instructions regarding preventceptive methods. The fundamentals of infertility study can be

carried out in the office. Immediate results often follow a thorough examination and assurance regarding the patient's potentialities for motherhood.

Tubal patency tests are usually done between the completion of the period and the time of ovulation. The passage of a sterile, dilute phenolsulfonphthalein solution through the tubes has proved to be a much safer, simpler, and less painful method than the use of carbon dioxide or air.

In general, pain arising from the ovaries is referred upward to the renal region; tubal pain tends to be off center and is often unilateral; uterine pain is centralized, frequently cramping in character, and radiates to the sacral area. Discomforts from bowel, bladder, and back may be attributed to the internal genitalia.

In the presence of unnatural genital bleeding there is a tendency for patients and physicians to delay pelvic examination. Procrastination prevents diagnosis. If there is any question of pregnancy, antiseptic cleanliness and gentle care should be used with speculum examination and with palpation. Uterine bleeding which cannot be associated with pregnancy, polyps, cancer, cervicitis, ovulation, or a tumor requires observation and consideration. An accurately kept menstrual chart and a pad-count are helpful. Endometrial biopsy or curettage may be of diagnostic value. Dysfunctional uterine bleeding may require treatment with thyroid, estrogens, or surgical curettage.

Sweat and sebaceous glands of the vulva are the usual source of bothersome genital odors. The treatment is soap and water cleanliness.

Endocervicitis causes a thick, tenacious, mucoid discharge. Office treatment consists of fulguration or

cauterization of the cervix, followed with the use of antiseptic suppositories or vaginal ointments.

Gonorrheal discharge is thick, purulent, and accompanied by inflammation of the urethra and cervix. Diagnosis is confirmed by culture. Treatment consists of temporary segregation, penicillin, and follow-up cultures until all evidence of the infection has cleared.

*Trichomonas vaginitis* causes a frothy discharge, punctate areas of vaginal ulceration, and the typical motile organisms which can be seen microscopically in a solution of saline. Systemic therapy consists of correction of anemia and direction of nutrition particularly with reference to adequate vitamin B. Local treatment can be carried out by the patient at home with a number of preparations — Allantomide vaginal cream, Triple Sulfa cream, Devegan Tablets, and Tetronyl Vaginal Jelly. One of these materials should be inserted into the vagina at night. A cleansing detergent douche in the morning, may be followed by a clear-water or vinegar-water rinse.

Yeast infections of the vagina and vulva cause a crumbly, thick, white discharge, inflammation of the vaginal and vulval mucosa, and itching. Diagnosis can be confirmed by suspending some of the discharge in saline to which a drop of NaOH, 10%, has been added. After 20 minutes the straw-like mycelium may be seen microscopically. The urine should be examined for sugar. Systemic treatment is as for trichomonas infections. Local treatment with Propion Jel or Tetronyl Vaginal Jelly applied at night should be followed in the morning by a detergent douche.

Through fear, ignorance and early conditioning many married women and their husbands fail to achieve a healthy emotional satisfaction from

their sex urges. Dyspareunia, vaginismus, lack of libido and sexual sadism form a part of office gynecology which has a higher psychiatric than physical component.

A pelvic tumor should not be compared in size with pregnancy. An accurate method of informing the patient about her tumor is to have her feel it abdominally or draw a picture of the tumor for her. When and why a tumor develops is usually unknown; admit this lack of knowledge and assure the patient that nothing she did brought about the new growth. Diagnosis can be more accurate after removal and microscopic section of the tumor.

#### THE CLIMACTERIC

The majority of healthy women pass through the climacteric without any disturbance in physical well-being and without any change in emotional stability. Cessation of menstruation before 40 is uncommon; other causes of amenorrhea are to be sought. Regular menstruation persisting after the age of 50 may be normal. However, due to the greater possibility of endometrial cancer in these women, a delayed menopause should be thoroughly investigated by examination and diagnostic curettage. Excessive and irregular bleeding during the climacteric call for a consideration of pregnancy, cancer, polyps, tumors—and estrogen medication.

Hot flushes, insomnia, and some degree of irritability are to be expected; when exaggerated, psychic factors are contributory. Fears, superstitions, and psychosexual changes gain prominence at the time of the climacteric. Such conditions as depressive psychosis, involutional melancholia, ill-defined pelvic pain, and undue anxiety are not a part of the aging process. Tendencies toward alcoholism frequently become overt at this time.

*Treatment of the Climacteric.* Adequate nutrition, careful grooming, and a healthy attitude of optimism have extended the period of middle age for American women. These factors are more important than estrogens. Rarely does a woman of today look old at 35. If the patient uses a contraceptive this practice should be continued for one year after menstruation stops.

Barbiturates should be used sparingly, never in large doses or over a long period of time.

Estrogens should be used in physiologic doses or not at all; they are not indicated in the treatment of psychiatric symptoms. Indications: to alleviate vasomotor symptoms, to relieve arthritic conditions secondary to hypo-ovarianism, and for local effects on atrophic tissues. For the relief of vasomotor symptoms a dosage of 0.2 to 0.5 mgm. of diethylstilbestrol, or 0.65 mgm. of estrone sulphate, or 0.02 mgm. of ethinylestradiol each morning, for a period of 20 days followed by a rest period of 7 to 10 days, is satisfactory. It may be necessary to repeat the cycle two or three times. Somewhat larger doses may be indicated for relief of arthritic symptoms.

In atrophic vulvovaginitis, local application of estrogen suppositories or the use of an estrogen ointment is more beneficial than systemic administration. Estrogens should never be used in anticipation of or for prevention of the menopause. Used in this manner, they simply prolong the climacteric. Large doses of estrogens by hypodermic injection represent a form of "endocrine shock" therapy, rarely indicated. Patients using estrogens over a prolonged period of time become dependent upon their effect.

Besides uterine bleeding, other evidences of overdosage of estrogen

are: leukorrhea, tissue edema, breast swelling, unwanted libido, and a state of tension. The occasional patient with benign, proliferative endometrium of the uterus and irregular bleeding at the climacteric benefits from 5 mgm. linguets of methyl testosterone absorbed beneath the tongue twice daily for 10 days. This type of medication should never be used over a prolonged period of time or in the patient in whom carcinoma has not been ruled out by thorough curettage.

#### THE POST CLIMACTERIC PERIOD

The older woman's gynecologic symptoms are essentially the same as those of the reproductive and climacteric periods except that there is no longer the fear of pregnancy.

Concern about cancer is increased. Vulval lesions require careful investigation particularly with reference to cancer, avitaminosis, systemic diseases, and allergic reactions.

A majority of older patients can tolerate plastic vaginal operations. However, many women can learn to wear a supporting pessary to correct cystocele and procidentia. The Gelhorn plastic pessary has been found to be very useful.

For no group of women is the periodic check-up examination more important than to these older women. They need and appreciate the attention of their physician. Health is their most important possession.

*Medical Records and Annals, 47, P. 586-593, 1953.*



#### Chronic Constrictive Pericarditis And Rheumatic Heart Disease

Diagnosis of this condition is very difficult when there is an association with rheumatic heart disease. In the 18 cases of constrictive pericarditis (proven to be such at operation or necropsy) a cause was clearly apparent in 3 cases only, namely, tuberculosis in 2 cases and the presence of a foreign body in one. Among the remainder, 5 cases were associated with rheumatic heart disease; they are described in detail; they were all men.

Two of the 5 patients improved by pericardectomy and had the physical signs of mitral and aortic valve lesions, although no history of rheumatism was obtained. The other 3 died without operation, and post-mortem examination showed a

grossly thickened adherent pericardium, causing constriction in all 3, and also rheumatic carditis with valvular lesions. All had considerable cardiac enlargement, obvious clinically, with greatly increased venous pressure, chronic pulmonary congestion, and increased pulse pressure; two patients had ascites.

It is not believed that constrictive pericarditis is necessarily of rheumatic origin. But it is also pointed out that a clinical diagnosis of constrictive pericarditis is not excluded by the co-existence of rheumatic heart disease, heart sounds of normal intensity, and considerable cardiac enlargement.

*A. J. Kaltman, et al, Am. Heart J., 45:201, 1953.*

## Diagnosis and Treatment of Hemorrhagic Disorders

*Normal hemostasis depends on the integrity of the vascular bed, the platelets and the blood coagulation system*

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When a local area of a person of a bleeding diathesis is traumatized, blood escapes into the surrounding tissues, and the injured blood vessels constrict and retract, closing their lumina, as the platelets aggregate and initiate clot formation with the aid of fibrin. The platelets also contribute a vasoconstricting factor, now believed to be of prime importance in hemostasis. Later the blood-vessel walls relax, leaving the clot and the tamponade produced by the engorged surrounding tissues as the hemostatic mechanism. Still later, the extravasated blood begins to undergo absorption, leaving the blood clot as the sole source of hemostasis. If the vascular bed is deficient (i.e., poor vasoconstriction), clot-formation alone may not stop the oozing and the bleeding time will be prolonged. If the vascular bed and tissue turgor are normal, but a

soft, friable deficient clot forms, the bleeding time will be normal; but an hour or hours later (when the blood-vessel walls have relaxed), the wound may resume bleeding (i.e., in hemophilia).

Normal hemostasis depends on the integrity of three complex factors—the vascular bed, the platelets and the blood coagulation system. These mechanisms function together to curtail blood loss. In hemorrhagic disorders, 1, 2 or 3 of these factors may be abnormal, depending on the severity of the underlying process.

From the clinical and laboratory data the hemorrhagic disorders may be divided into (1) vascular dysfunction, (2) platelet deficiency, and (3) dysfunction in the coagulation system.

Hereditary telangiectasia, senile purpura, allergic, toxic and simple purpura, scurvy, and pseudohemo-

philia are the representative diseases in this group. The diagnosis depends on the history (i.e., familial in hereditary telangiectasia, exposure to a toxic agent in toxic purpuras, deficient ascorbic acid intake in scurvy, and a congenital or familial bleeding history in pseudohemophilia). Physical findings referable to the presenting vascular lesion, and adequate normal platelets, and a normal coagulation mechanism as shown by laboratory tests complete the diagnostic picture.

Capillary fragility and bleeding-time tests in hereditary telangiectasis are normal. In the nonthrombocytopenic purpuras (allergic, toxic, simple or senile) these tests may or may not be abnormal. In scurvy the capillary fragility test is markedly positive while the bleeding time is normal. In pseudohemophilia the bleeding time is prolonged. A prolonged bleeding time with normal capillary fragility may also be encountered in some cases of idiopathic thrombocytopenic purpura after splenectomy.

The allergic, toxic and simple purpuras are usually self-limiting. Ascorbic acid produces dramatic results within 3 to 5 days in scurvy. Supportive transfusions are needed in pseudo-hemophilia.

A simple test for the evaluation of thrombocytopenia is the perusal of a routine blood smear. Normally one sees 1 to 5 platelets with an occasional clump in every oil-immersion field. When the platelet count is 50,000 or below, a rare, large individual platelet is found in every fifth or tenth field. This finding, and the absence of clot retraction, is sufficient for the diagnosis of thrombocytopenia, and these tests should always be performed to check the platelet count.

In children and young adults idiopathic thrombocytopenic purpura tends to occur following an upper

respiratory infection or after one of the acute infectious diseases of childhood. Cortisone is to be given for 10 to 14 days; platelet transfusions as necessary, observation for many months. When a severe acute case or a chronic case of this disease is not responding to supportive therapy, splenectomy may produce marked amelioration or cure of the thrombocytopenic process.

In the secondary thrombocytopenias removal of the offending agent or disease may effect a cure. If persistent and troublesome, splenectomy is indicated, after a trial of cortisone therapy.

In the group characterized by defect in the blood coagulation system, with normal platelets and normal vascular function, coagulation of whole blood and recalcified plasma is abnormally prolonged, utilization of prothrombin poor. The Quick prothrombin test is normal in hemophilia, markedly decreased in hypoprothrombinemia (i.e., with dicumarol therapy), parahemophilia (Ac globulin is significantly reduced) and congenital SPCA deficiency; no clotting endpoint occurs in fibrinogenopenia.

Bleeding in hemophilia, parahemophilia and SPCA deficiency may be mild, moderate or severe. Hemarthroses are common in hemophilia and rare in the few reported cases of parahemophilia and SPCA deficiency. Hemophilia is limited to the male sex; the other two occur in both sexes. Bleeding in liver disease is due to a decrease in prothrombin and SPCA. The abnormal Quick prothrombin activity in patients with parenchymal liver disease will not be affected by the parenteral (or oral) administration of vitamin K oxide, whereas the abnormal Quick prothrombin activity in patients with obstructive jaundice will return to normal when vitamin K oxide is administered IV.

Blood should be drawn for the necessary tests before transfusions are administered.

In medicinally induced hypoprothrombinemia 50 to 100 mg of vitamin K oxide IV will reduce prothrombin activity to a safe level in a few hours. Protamine sulfate, 200 to 300 mg. IV, will neutralize the excess heparin where heparin is used as the anticoagulant. Cohn's plasma fraction 1 contains fibrino-

gen, of value in the treatment of fibrinogenopenia, congenital or acquired.

Patients with circulating anticoagulants are supported with blood transfusions. A trial of cortisone or ACTH is indicated here in accordance with the proposals that some of these anticoagulants may be antibodies.

*Med. An. D. C., 22:414-417, 1953.*



### **Carbohydrate Metabolism in Obesity**

A study was made of 12 obese women (and also of normal controls) in an attempt to determine whether a correlation could be discerned between the phase of obesity and the pattern of glucose tolerance. Deviations from normal in the carbohydrate tolerance of obese individuals, if they exist, are likely to be small. The subjects of this study were regarded as being in the "active" phase of obesity if they had been gaining appreciable amounts at the time of study, or if their condition was of relatively recent onset.

"Static" obesity was defined as that of long duration with weight gain arrested for long periods. Two types of carbohydrate tolerance

study were carried out on each subject, and caloric, protein, carbohydrate, and fat content of self-selected meals were calculated in each case. The six women in the active phase of obesity approximated the food intake of six normal-weight controls, while the women in the static group had a significantly smaller carbohydrate intake than their controls.

The group in the category of active obesity displayed markedly increased tolerance both to glucose and to dietary carbohydrate compared with its control group. On the other hand, the obese women in the static phase displayed normal or decreased tolerance to the substances.

*R. Baudoin, et al, J. Clinical Nutrition, 1: 91, 1953.*

## Acute Pharyngitis

*Diagnosis of infectious mononucleosis  
should be excluded by a white count with adequate  
examination of the blood smear*

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J. F. WALDO, M.D., Salt Lake City, Utah

It is estimated that acute pharyngitis is the third most common cause of absenteeism among workers. The most common pharyngitis is the virus sore throat. The throat may be slightly edematous and reddened, but usually there is little more than symptoms for a diagnosis. This type of sore throat is not amenable to treatment with the antibiotics and is usually handled best by local therapy and by treatment of the disease with which it is found to be associated.

For acute strep. pharyngitis penicillin is the drug of choice; give enough for adequate good levels for 5 to 7 days.

A common form of acute pharyngitis is that caused by the Vincent organisms. There are spotty soreness in the throat and punched-out ulcers with ragged edges. Smears from the ulcer stained with gentian violet, the large spirochetes and the fusiform bacteria are usually seen; us-

ually there is adenitis and moderate toxicity. Ordinarily well managed with penicillin, if resistant, marpharsen IV gives dramatic results.

Perhaps most frequently undiagnosed is the sore throat of infectious mononucleosis; this may simulate any other form. Frequently throat is beefy-red, occasionally small ulcerated areas or membrane as of diphtheria. Differentiate by diffuse adenopathy of neck and other areas of the body, and in many cases a palpable spleen, confirmed by the abnormal blood findings. Not infrequently one sees a strep. pharyngitis with this disease. Patients with infectious mononucleosis are prone to suffer relapses and a long-drawn-out course if they are not confined to bed during the active stage.

Syphilis may produce a pharyngitis in its secondary or late tertiary phase. The throat shows ragged ulceration, is moderately red, may be an exudate over the posterior

pharynx. Cervical adenopathy not severe. STS confirms. This sore throat responds promptly to penicillin. Every leucitic should receive adequate treatment.

In any chronic sore throat cancer should be looked for.

The ordinary severe pharyngitis should have a throat culture and smear, a white count with adequate

examination of the blood smear to exclude infectious mononucleosis, and an STS. The exact etiology should be determined early because in diphtheria and strep. pharyngitis the time element is far more important than the dose of the therapeutic agent.

*Rocky Mountain Med. Jour.*, 50:8, 670, 1953.



### **NPH-50 Insulin, Its Nature and Uses**

NPH (neutral-protamine-Hagedorn) insulin's action is between the rapid, short effect of regular insulin and the slow, prolonged effect of protamine zinc insulin. By releasing insulin more rapidly in the first 12 hours after injection (the hours during which the patient has his meals), it exerts sufficient action over the day, while, in most cases, avoiding both hypoglycemic reactions and postprandial hyperglycemia at the peak (or maximal effect duration).

NPH-50 should be injected before breakfast subcutaneously, never cutaneously, IM, or IV. Effect is noted, usually in 5 or 8 h., may be after 2 or 3 h., especially if not given entirely in one subcutaneous depot. The action continues for some 20 hours at its most effective range, then with less intensity for a total action of 24, even 32 h. It is thus a stable, neutral, more constant mixture in "permanently" bottled form acting like the 2:1 (2 regular to 1 PZ).

NPH-50 is not intended to replace all other types of insulin. Regular insulin still remains the choice for emergencies, for ketosis and coma, for uncertain food intake, etc.

The ideal indications for NPH-50 insulin are the same as for the 2:1

insulin mixtures, i.e., cases not controlled by globin zinc insulin or PZ insulin alone. While PZ insulin has been combined with any proportion of regular insulin, experience has tended to indicate the use of 2:1 mixture in most cases, and this is the most readily replaced by NPH-50 insulin.

For a patient on less than 40 units of a long-acting insulin or a "mixture," it is generally well to order the same number of units of NPH. If the patient is getting over 40 units of a "mixture," the initial NPH dose should equal all of the PZ insulin plus 80% of the regular insulin.

Patients should be instructed that the early symptoms of a hypoglycemic reaction due to NPH-50 insulin are vague and may not be as distressing as the reactions from other insulins. Nevertheless, the usual corrective measures must be promptly instituted, if otherwise unexplained fatigue, headache, lassitude or drowsiness occur. The late symptoms are the more well-known weakness, sweating, tremors, hunger, "nervousness," central nervous system changes, psychiatric disorders, and loss of consciousness.

Benj. Ashe, *New York State Jour. of Med.*, 53:1539, 1953.

## General Practitioners Should Treat Alcoholism

*Almost dramatic results can be obtained  
in a large percentage of cases with a simple,  
logical and safe treatment*

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R. G. McALLISTER, DeKalb, Illinois

Treatment of 90% of alcoholics is well within the scope of the G.P. Almost dramatic results can be obtained in a gratifying percentage with a simple, logical and safe treatment. Although one occasionally sees a rowdy and disagreeable alcoholic, the treatment most frequently is pleasant.

Adrenal Cortex Extract (ACE), combined with Vitamin C and also Vitamin B Complex, can produce almost dramatic results in the alcoholic who wants relief. It is rarely necessary to give more than one, or probably two, injections a day until the patient is under control. Frequently he can make it to the office the second day, for by that time he has noted definite relief and is co-operative and eager for further treatment.

The IV injection of 2 c.c. of ACE, combined with 500 mg. of Vitamin C and 1 c.c. of a strong B Complex solution, is made daily, until the

pulse and b.p. approach an expected normal, the tremor is gone, the patient is smiling about his "best night's sleep in two months" and complaining about how much and how often he eats. Two, five or six days treatment may be required for such result.

From this time on, he comes to the office, at first daily, then every two days, then every three, then weekly, and so on, for an injection of  $\frac{1}{2}$  c.c. of Lipo-Adrenal Cortex—a more lasting and potent solution of the hormone—this, with only an occasional medical check-up.

Other medication should be used with the hormone. Mephenesin, 1 gram every two hours, is most helpful for the general tension and tremor, especially for the first three or four days of withdrawal of alcohol. Potent preparations of Vitamin C and Vitamin B Complex are given orally from the first. Mild sedatives are usually sufficient, as Dormison

or chloral hydrate in moderate doses; rarely paraldehyde may be necessary at first.

After a week of the Vitamins C and B Complex, the patient is put on a complete vitamin-mineral preparation in as large doses as he will tolerate, and this should be maintained indefinitely.

A prime essential is the understanding, sympathetic interest of the physician, and his continued encouragement. The same family-doctor approach that applies to other diseases works with the alcoholic.

Fill the void with something at least as strong and as consuming. Active participation in Alcoholics Anonymous, through fellowship with others who have been over the same road, can find a program which can direct him toward a definite rehabilitation. Resuming activity in his church will often reestablish his self-respect and give him needed spiritual aid.

An understanding of his problem by his wife and family is essential to recovery.

R. G. McAllister, *Medical Times*, 81:536, 1953.



### A.C.T.H. in Delirium Tremens

Two cases of delirium tremens were treated with A.C.T.H. and results were rapid and favorable in both cases.

A man, 30, entered hospital delirious and with the usual hallucinations. The attack may have been precipitated by a wound on the back of the r. hand which severed one of the extensor tendons. In a few days, after treatment with sedatives, vitamin-B complex orally, and large doses of vitamin B<sub>1</sub> parenterally, the mental condition had improved and it was decided to suture the cut tendon. Thiopentone was given IV and operation was completed in 18 min. From this day patient sank into a state of low muttering delirium; t. 100 to 103, completely disorientated as to time and place. Blood films negative for malarial parasites. He frequently went through the "rope-climbing" movements which are said to be typical of serous "meningitis" (wet brain). Lumbar puncture produced normal cerebro-

spinal fluid at a pressure of 110 mm. Penicillin, streptomycin, and sulphadiazine had no effect on the fever. 14 days after the operation it was decided to try 20 units of A.C.T.H. q. 6 h. After two doses the mental condition was almost normal, in 24 h. he was perfectly sane, t. normal and convalescence was rapid after that. The A.C.T.H. was gradually reduced to 5 units once daily, and this was continued for three days and then stopped.

A woman, 57, admitted to hospital in subacute delirium, completely disorientated as to time and place, restless, t. 98 to 100. After 24 h. she was given 40 units of A.C.T.H. every 8 h. and after one dose the mental condition was almost normal. Recovery was rapid and the patient discharged in 6 days. The A.C.T.H. was stopped after 4 days, by which time it had been reduced to 20 units once daily.

S. C. Bettencourt-Gomes, *British Med. Jour.*, 4831: 342, 1953.

## CASE REPORT

### Case Records of the Massachusetts General Hospital

*A 51-year-old housewife was admitted to hospital because of the sudden onset of vomiting, unresponsiveness and paralysis of the right arm and leg;*

her husband said that she had been well, though obese, until 10 years before admission, when she had an episode of vomiting and collapse and was taken to a hospital, where she was told that she had pneumonia and a nervous breakdown. No paralysis was noted, but afterward she was less energetic and tired more easily. Eight years before admission she was hospitalized because of sudden paralysis of her right side. This gradually cleared over several weeks, with little residual weakness. Five years before admission she was given digitalis because of dyspnea. Recently, she had been taking one tablet of digitoxin daily. Three years before admission paralysis of her right side again suddenly developed, decreasing gradually for several weeks but never entirely clearing. Since that time she had been childish.

One year before admission exertional dyspnea became severe and nocturnal dyspnea, ankle swelling and "swollen neck veins" were noticed for the first time. She was hospitalized for "palpitations," and at that time diabetes was discovered. Glycosuria had been controlled by diet, and she had lost 20 pounds in the past year. During this hospitalization she was given nitroglycerin for infrequent pain in the anterior chest, always with prompt relief. The chest pain was unrelated to exertion. At the onset of paralysis, 16 hours before admission, she vomited and became unresponsive and incoherent. Dyspnea increased and she perspired profusely.

The patient was acutely ill, stuporous, cyanotic, tachypneic, somewhat obese and moaning constantly. The neck veins were distended but not pulsating. There were moist

rales over the lung bases and a post., apical beat was felt 11 cm. to the left of the midsternal line in the 5th space. Auricular fibrillation, vent. rate 160. Questionable diastolic gallop at apex. The heart sounds seemed of normal intensity, partly obscured by noisy breathing; the aortic second sound equaled the pulmonic. The liver border was firm and smooth, four fingerbreadths below the costal border, 2-plus pitting edema of the ankles and sacrum. The right radial, r. femoral and both pedal pulses were not palpable, but the extremities were warm.

There was a loss of l. lateral gaze, and corneal reflexes were present, pupils were equal and did not react to light, fundi normal. Tongue was in midline, gag reflex was present; no response to pinching. Complete flaccid paralysis of the r. arm and leg. Deep tendon reflexes of both arms and legs was absent. Hoffmann reflex on the right and absent on the left. R. plantar reflex was absent.

Pulse 160, temp. 100.2° by rectum, resp. 40. B.P. 105/90, urine cloudy, orange, acid, 4-plus albumin, a green test for sugar and a 1-plus to 2-plus test for bile. Sediment contained 8 to 10 white cells, occasional hyaline, granular and red cell casts and many bacteria per h.p. field. White blood cell count 16,900, 85% neutro., 14 lymph., 1 mono., hgb. 18 gm. per 100 c.c., hematocrit 60%. Fasting blood sugar 236 mg. per 100 c.c., prothrombin time 40%, nonprotein N. 44 mg. per 100 c.c., sodium 138 and chloride 108 milli-equalivalent per liter. Spinal fluid pressure 230 mm. of water; 15 c.c. of clear, colorless fluid removed, and final pressure 180 mm. of water. The fluid contained 4 lymphocytes, 1 neutro. and 12 red cells per c.m. The ammonium sulfate test was negative.

Two hours after admission the patient vomited 20 c.c. coffee-colored

material of 3-plus guaiac reaction. Next day the patient was still unresponsive, sweating profusely; b.p. 85 sys, by palpation, P. 80, still auricular fibrillation; t. 102.5° by rectum. There were moist rales at lung bases, more prominent, distinct diastolic rumble at the apex. Later that day b.p. and pulse became unobtainable, cyanosis deepened; resp. grew very weak, heart rate slowed to 40 per min., r. pupil was larger than l., and both reacted sluggishly to light. Eyes moved in all directions when the head was moved. The patient died 42 hours after admission.

#### DISCUSSION

*Dr. Briant L. Decker:* This 51-year-old woman, in the eight years before admission to the hospital, had had three cerebrovascular accidents, and in the previous 5 to 10 years had evidence of congestive heart failure. She entered the hospital in her terminal illness in coma with a right hemiplegia and congestive heart failure.

She had rheumatic heart disease with mitral stenosis. I base this opinion on the apical diastolic rumble heard terminally, the auricular fibrillation, and the long history of congestive heart failure. With this diagnosis as a basis, it might be assumed that the fibrillation was of at least eight-years' duration and that the cerebrovascular accidents of eight and three years previously were on an embolic basis.

The suddenness of onset of both attacks and practically complete recovery from the first, and fairly good recovery from the second, fit in the embolic phenomena. The fact that she never regained her former personality after the second cerebrovascular accident is consistent with that explanation. It is reasonable to suppose that the final apoplectic attack was also embolic and

that a large portion of the left middle cerebral artery was involved. The normal spinal fluid is against cerebral hemorrhage, although the terminal events suggested increase of intracranial pressure; likewise, the absent pulsations in the peripheral arteries may be explained by emboli from the left atrium.

The bile in the urine, the prothrombin time of 40% and the urinary findings could have been the effect of chronic congestive heart failure on the liver and kidneys, but I doubt if the hemoglobin of 18 gm. and the hematocrit of 60% can be explained by congestive heart failure due to mitral stenosis. I believe the most likely possibility is that the patient also had tricuspid stenosis. A typically localized murmur was not described, but it is often indistinguishable from that of mitral stenosis and the two occur together.

Could the cerebral episodes and the bouts of congestive heart failure have been due to polycythemia vera? Against this theory is the absence of an enlarged spleen. I should think that with polycythemia vera of this duration the hemoglobin and hematocrit would have been at a higher level. I believe the polycythemia was secondary.

Since the patient had diabetes, may it not be reasonable to suppose that, in addition to the mitral stenosis, she had considerable arteriosclerosis, and that the absent pulsations in the extremities and at least the final cerebrovascular accident were on an arteriosclerotic basis, and that the terminal coma and hemiplegia were due to progressive thrombosis? She felt pain in the an-

terior aspect of the chest which was relieved by nitroglycerin. Therefore she may have had a myocardial infarct in her final terminal congestive heart failure, which produced cerebral thrombosis by precipitating a marked drop in the blood pressure. Against these explanations are the facts that the diabetes was mild and was controlled by diet, and the fundi were reported as normal. The sudden onset of the final accident is more suggestive of an embolus or hemorrhage than of thrombosis. There was no history of chest pain before the paralysis and no ECG was mentioned in the protocol. Consequently, the pain must have been significant. With the duration of the case history, a brain tumor is unlikely as an explanation of the cerebral symptoms.

I believe that this patient had rheumatic heart disease with mitral stenosis and auricular fibrillation, giving rise to cerebral and possibly to peripheral emboli. I further believe that before admission the patient was in congestive heart failure, was fibrillating, and had a fairly large embolus lodged in the left middle cerebral artery, which produced right hemiplegia and coma.

#### AUTOPSY

*Anatomical Diagnoses:* Rheumatic heart disease, with mitral and aortic stenosis.

Mural thrombosis, left atrium, with recent emboli to right internal carotid and superior mesenteric arteries. Cerebral infarcts, recent and old. Thrombosis, old, probably embolic, of abdominal aorta.

From *The New England J. of Medicine*, 9-17, 24, 1953, with the kind permission of the Editor.



## DISCUSSION ON HYPERTENSION

Hypertension means a systolic b.p. of 150 or more, or a diastolic p. of 95 or more. For the purpose of life assurance, maximum readings usually accepted at ordinary rates are: for age up to 50 years 145/90; for age over 50 years 155/95.

Four factors most helpful in the assessment of the prognosis of essential hypertension are: (1) The diastolic pressure reading. (2) Evidence of cardiac failure. (3) Evidence of renal failure. (4) Ophthalmoscopic appearance.

Diastolic pressure is probably the most important single factor in assessing the prognosis, the critical level is about 135. Above this figure, the prognosis is bad and a cerebral vascular lesion is likely to occur. With a diastolic pressure of less than 100, the prognosis is good. One frequently sees in practice patients with a pressure of the order of 200/95, which usually indicates a benign condition, the high pulse pressure being due to degeneration of the elastic tissue in the arterial system.

Dyspnoea on exertion, the presence of fine rales at the bases and an accentuated pulmonary second sound indicate left ventricular failure. Cardiac asthma is a symptom of grave import and a patient rarely lives more than two or three years after its onset.

Symptoms of uraemia, a raised blood urea and the presence of albumin and casts in the urine, all indicate a grave prognosis. One of the best tests of renal function is the ability of the kidneys to excrete a concentrated urine. All that need be done is to withhold fluids for 12 hours and then to determine the sp. gr. of the urine that is passed at the end of this period.

**Ophthalmoscopic**—Look for uneven calibre of the retinal arteries, nipping of the veins at the arteriovenous crossings, exudates in the retina and papilloedema. Age, family history, occupation, temperament and habits regarding alcohol and tobacco, must be taken into account in formulating a prognosis.

Another group of patients are those with a high pressure, maybe severe symptoms, retinopathy or evidence of cardiac or renal failure. A diastolic pressure of over 120 is a cause for anxiety.

A few days' rest in bed with sedatives frequently reduces the p. by 10 or 15 mm. and relieves symptoms. A low-sodium diet appears to produce a fall in b.p. in 25% of cases. It is used in the treatment of severe hypertension without evidence of renal failure. A diet containing 2,000 calories and 200 mg. of sodium is suggested.

For halogen salts of hexamethonium and pentamethonium good results have been claimed when given by injection, but oral administration seems to be unreliable. Toxic effects are common and include pupillary paralysis, nausea, constipation, paralytic ileus and bromism. I have had no success in the few patients I have treated with hexamethonium orally, but it did relieve hiccoughs in a patient with secondary carcinoma of the liver when everything else had failed.

I have treated two patients with a combination of Veriloid and phenobarbitone, either 3 or 4 tablets daily, (2 mg. veratrum viride and  $\frac{1}{4}$  gr. phenobarbitone.)

It is difficult to decide whether or not Veriloid therapy is of benefit.

Leslie V. Gimson, in *Proc. Royal Soc. of Med.* (Lond.) Sept., 1953.

## AIDS IN DIAGNOSIS

### Tubeless Gastric Analysis

Diagnex® (Squibb) is a cation exchange resin, consisting of Amberlite XE-96 and quininium; the latter is combined with carboxylic acid groups as an indicator cation. In the presence of free hydrochloric acid a cation exchange takes place and quinine is liberated. Segal, *et al* (*Gastroenterology*, 16: 380, 1950) described a test whereby this reaction could be applied to the recognition of free hydrochloric acid in gastric juice, thus rendering intubation unnecessary; the displaced quinine is absorbed in the small intestine and excreted in the urine.

The fasting subject swallows a standard quantity of "Diagnex" (2 gm) and urine is collected hourly for 3 hours. Quinine is extracted from each urine specimen with ether and acid using the method of Kelsey and Geiling (*J. Pharmacol.*, 75: 183, 1942). The extracts are compared with a standard quinine solution in a fluorimeter and the total quinine content of each specimen is calculated.

Clinical trials have confirmed the work of Segal *et al*. The test indicates accurately the presence or absence of free hydrochloric acid in gastric juice. "Diagnex" itself does not provoke hydrochloric acid production and, in the absence of spontaneous acid secretion, a potent stimulant such as histamine must be

used concurrently. Achlorhydria was proved in 12 subjects, 9 of whom were known to have achylia gastrica; in this group, the quinine excretion never exceeded 15.8 ug. in any specimen. On the other hand, 6 subjects who were suffering, or had suffered, from peptic ulceration, excreted 21-131 ug. per specimen. Mean curves show that these two groups of cases are clearly differentiated.

Attempts are being made to use "Diagnex": (a) to test the efficacy of ganglion-blocking agents on acid secretion; (b) to estimate acid output after gastrectomy, and (c) to compare its value as an indicator with Topfer's and Günzburg's reagents.

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H. Conway, *et al*, *J. Physiol.*, 121:41, 1953.

### Appendicitis or Ureteritis (Pyelitis)?

As urinary infection is a common cause of abdominal pain in infants, children and young women, the physician should explore the possibility of such infection before he decides the symptoms are caused by an inflamed appendix which should be removed.

The blue litmus test, employed at the bedside to gauge the acidity of the patient's urine may appear crude and outmoded, yet no diagnostic procedure yields great dividends, to both the physician and the patient.

The physician is secure in the correctness of his diagnosis; the patient may be spared an unnecessary operation. If the disease is ureteritis, the patient will receive specific treatment for this common disorder and may thus escape painful and disabling disorders of the genitourinary tract which often follow untreated ureteral infections.

In much of the literature dealing with inflammation of the ureters, the term "pyelitis" is used to indicate ureteral infection. "Pyelitis" should be confined to inflammations of the pelvis of the kidney. "Ureteritis" is the proper term for inflammation of one or both ureters.

Ureteritis accounts for most discomforts in the lower portion of the abdomen in young girls. As colon bacilli thrive only in acid media, alkalization usually brings prompt recovery from ureteral inflammation.

L. L. Craven, *Mississippi Valley Med. Jour.*, 75:134, 1953.

### **The Ear Lobe As A Source Of Blood In Hemoglobin Estimation**

The main conclusions drawn on the basis of the comparative measurements of samples of capillary blood from the root of the finger nail and the lobe of the ear as against heparinized venous blood from the arm, are as follows:

1. Capillary ear-lobe blood has a higher mean hemoglobin concentration than capillary blood from the root of the nail (except in the morning before breakfast).
2. The coefficient of variation of ear readings is higher than that of finger readings (except in the morning before breakfast).
3. Mean hemoglobin values for capillary blood from the finger and for venous blood from the arm are not significantly different.

The most interesting finding was that the hemoglobin concentration of ear-lobe blood varies with the serial drop from the same puncture; early drops had a significantly higher content than later drops. There was no significant difference between serial finger drop values.

These measurements on serial drops from fingers and ears were repeated in a more heterogeneous group of students, 17 women and 23 men. The conclusions derived from the previous experimental group were confirmed.

It is suggested that the use of the ear-lobe as a source of blood for the estimation of hemoglobin concentration should be strongly discouraged.

A. S. Henderson, *J. Physiol.*, 121:43P, 1953.

### **Amebic Hepatitis Presenting as Fever of Unknown Origin**

The difficulty in arriving at the diagnosis in the two cases presented should not be construed as support for a therapeutic test with amebicidal drugs in cases of obscure fever. The known toxicity of emetine and the nonspecificity of chloroquine preclude such an approach to the management of obscure fever. The recognition, however, that fever of unknown origin may be due to amebic hepatitis will lead to the appropriate diagnostic studies and their careful evaluation. The failure to find *E. histolytica* in the feces does not exclude early amebic hepatitis.

Two patients with hepatic amebiasis presenting as obscure fever are described. In both the diagnosis was established only after long delay. Amebiasis should be included in the diagnostic consideration of fever of obscure origin. The complement-fixation test in amebiasis is a valuable diagnostic procedure.

Heller, P., et al, *New Eng. Jour. of Med.*, 249:397, 1953.

## THERAPEUTIC TRENDS

### **Treatment Of Nephrotic Syndrome With Interrupted ACTH Or Cortisone Therapy**

Sixteen patients with nephrotic syndrome received corticotropin, but 11 of them experienced a relapse with drop in serum complement level within the period of 12 months. Five of 6 children given maintenance therapy with corticotropin did not relapse, and the serum complement remained within the normal range. Another group of 3 patients who received corticotropin during the initial week of treatment and then were interruptedly treated with oral doses of cortisone was able to remain free of edema and maintain a normal serum complement level. In one patient the urine was kept free of abnormal constituents and in 2 others there was a marked decrease in albuminuria. Blood cholesterol levels returned to normal in all three patients.

k. Lange, et al, *Proc., Soc. Exper. Biol. & Med.*, 82:315, 1953.

### **Control Of Hypertension With 1-Hydrazinophthalazine (Apresoline)**

The effect of "apresoline" on hypertension was studied in 65 patients. An initial dose of 50 mg. of the drug was given by mouth three or four times a day, after which it

was gradually increased until a desired effect was obtained or intolerance developed. In 31 out of 41 patients suffering from benign essential hypertension there was a fall in both systolic and diastolic blood pressure of 20 mm. Hg. or more, 16 of these patients remaining normotensive for four to twenty weeks. The ten patients who responded poorly had mostly a long history of hypertension with permanent vascular damage and renal involvement. In only one of the 9 patients with hypertension believed to be of renal origin was there a fall in pressure of more than 20 mm. Hg. In two of six patients with malignant hypertension the results were excellent, the blood pressure falling nearly to normal with a reduction in albuminuria and papilloedema. Sympathectomy had previously been performed without a satisfactory result in three patients and in one of these blood pressure returned to normal. In thirty of the sixty-five patients no significant side effects were observed, but ten ceased treatment on account of toxic reactions, which included headache, nausea, vertigo, drowsiness and nervousness.

It is concluded that apresoline is an effective agent for the short-term control of blood pressure in certain cases of essential hypertension and malignant hypertension.

S. S. Riven, et al, *Am. J. Med.*, 14: 160, 1953.

## Acute Postoperative Dilatation Of The Stomach

The usual sequence in bringing about this dilation is as follows: the adrenocorticosteroid reaction causes sodium retention and potassium excretion; vomiting or gastric aspiration cause dehydration, thus increasing alkalosis (due to chloride loss) and increasing potassium loss; the condition may be further aggravated by the intravenous infusion of inappropriate saline solutions.

The development of alkalosis may be clinically anticipated by watching for the following changes in the gastric juice: (1) the quantity is increased in excess of 120 cc. per hour; (2) translucency is replaced by turbidity (as pepsin activity is inhibited), with an increasingly foul odor; (3) the color of the juice changes from clear to bile-stained to green, yellow, feculent and brown, in sequence; (4) the total chloride content and pH rise. The quantity and translucency of the gastric juice are the most useful clinical guides and have been found to correlate with the carbon dioxide combining power.

The immediate purpose of treatment is to restore the circulating blood volume and urinary output; blood, serum, or dextran are administered for shock. The next objective is restoration of the ionic balance of plasma, which is done by intravenous infusion of chloride and potassium, and of the alimentary tract, which is done by administering sodium, potassium and chloride by mouth through an indwelling gastric tube. Only the minimal requirements of these electrolytes must be administered intravenously, special precautions being taken with potassium. The gastric tube is withdrawn and feeding by mouth restored when the gastric juice has again become translucent and there is no evidence

of retention. Supplementation of the diet with sodium, potassium and chloride is necessary during the early phase of oral feeding, and should be continued until the body stores are adequate to provide the electrolytes needed for digestion.

K. W. Starr, *Ann. Roy. College Surg.*, 12:71, 1953.

## Circulatory Effects Of Aminophyllin In Acute Myocardial Infarction

Aminophyllin is widely used in the management of acute myocardial infarction as a coronary dilator and to alleviate cardiac failure. The effects of 0.25 to 0.5 gm of aminophyllin given intravenously over a 10-minute period have been studied in 5 patients with acute myocardial infarction. Cardiac output was measured at the bedside by the dye dilution technic, and arterial pressures were recorded with a strain gage manometer. Venous pressure changes were determined with a saline manometer.

In 3 patients with satisfactory repeat output determinations no clear-cut change was observed. All three had initial cardiac indices in the normal range. The dye circulation times were shortened in two of these patients (36 to 27, and 23 to 16.5 seconds). In the third patient it rose from 18 to 21 seconds. In 4 patients the arterial pressure fell about 10 mm. Hg. towards the end of the injection and quickly rose to control levels or higher in 3. The venous pressure fell in each case. There were no significant rate changes.

No untoward effects were noted. It may be concluded that when given cautiously, aminophyllin need have no significant depressor effects in acute myocardial infarction. Venous pressures were improved.

R. P. Gilbert, *Clinical Research Proc.*, 1:80, 1953.

## FREE LITERATURE SERVICE

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### Allergies

allergic reactions<sup>1</sup>, asthma<sup>2</sup>, asthma (bronchial)<sup>3</sup>, drug sensitivities<sup>4</sup>, eczema<sup>5</sup>, food<sup>6</sup>, hay fever<sup>7</sup>, urticaria<sup>8</sup>.

### Blood, Cardiovascular

anemia<sup>9</sup>, anemia (pernicious)<sup>10</sup>, anticoagulant<sup>11</sup>, arteriosclerotic peripheral vascular disease<sup>12</sup>, angina pectoris<sup>13</sup>, Buerger's disease<sup>14</sup>, cardiovascular disorders<sup>15</sup>, congestive heart failure<sup>16</sup>, cardiac asthma<sup>17</sup>, coronary artery<sup>18</sup>, coronary thrombosis<sup>19</sup>, chronic trench-foot<sup>20</sup>, dietetic restriction<sup>21</sup>, hypertension<sup>22</sup>, myocardial failure<sup>23</sup>, myocardial insufficiency<sup>24</sup>, peripheral neuritis<sup>25</sup>, Raynaud's disease<sup>26</sup>, thromboangiitis obliterans<sup>27</sup>, varicose vein<sup>28</sup>.

### Dermatology

acne<sup>29</sup>, athlete's foot<sup>30</sup>, bacterial dermatologic condition<sup>31</sup>, bed sores<sup>32</sup>, burns<sup>33</sup>, dermatoses<sup>34</sup>, eczema<sup>35</sup>, external ulcers<sup>36</sup>, fungus diseases<sup>37</sup>, infections<sup>38</sup>, ivy dermatitis<sup>39</sup>, pruritus<sup>40</sup>, topical infections<sup>41</sup>, yaws<sup>42</sup>.

### Endocrinology

adrenal gland<sup>43</sup>, cretinism<sup>44</sup>, diabetes<sup>45</sup>, exophthalmic goiter<sup>46</sup>, Graves' disease<sup>47</sup>, hyperthyroidism<sup>48</sup>, myxedema<sup>49</sup>, pitu-

itary gland<sup>50</sup>, thyroid gland<sup>51</sup>, thyrotoxicosis<sup>52</sup>.

### Eye, Ear, Respiratory

bronchitis<sup>53</sup>, choroiditis<sup>54</sup>, coughing<sup>55</sup>, eye infections<sup>56</sup>, ear infections<sup>57</sup>, iritis<sup>58</sup>, keratitis<sup>59</sup>, laryngitis<sup>60</sup>, nasal congestion<sup>61</sup>, night blindness<sup>62</sup>, otologic dermatosis<sup>63</sup>, pharyngitis<sup>64</sup>, respiratory infections<sup>65</sup>, sympathetic ophthalmia<sup>66</sup>, sinusitis<sup>67</sup>, tonsillitis<sup>68</sup>, uveitis<sup>69</sup>, visomotor rhinitis<sup>70</sup>.

### Gastrointestinal, Liver and Spleen

amebiasis<sup>71</sup>, colitis<sup>72</sup>, constipation (chronic)<sup>73</sup>, cirrhosis of liver<sup>74</sup>, constipation<sup>75</sup>, diarrhea<sup>76</sup>, gallbladder and bile ducts<sup>77</sup>, gastrointestinal spasm (functional)<sup>78</sup>, gastroduodenal bleeding<sup>79</sup>, peptic ulcer<sup>80</sup>, staphylococci<sup>81</sup>, streptococci<sup>82</sup>.

### Genito-Urinary

bladder diseases<sup>83</sup>, cystitis<sup>84</sup>, kidney diseases<sup>85</sup>, prostate gland<sup>86</sup>, pyelitis<sup>87</sup>, ureter diseases<sup>88</sup>, urinary tract infections<sup>89</sup>, urethra diseases<sup>90</sup>.

### Geriatrics

anemia<sup>91</sup>, arteriosclerosis<sup>92</sup>, cardiac edema<sup>93</sup>, chronic fatigue<sup>94</sup>, climacteric

(male) <sup>95</sup>, constipation <sup>96</sup>, insomnia <sup>97</sup>, low blood sugar level <sup>98</sup>, protein deficiency <sup>99</sup>, senility (male) <sup>100</sup>, senility (female) <sup>101</sup>, vitamin deficiencies <sup>102</sup>.

## Gynecology and Obstetrics

amenorrhea <sup>103</sup>, cervicitis <sup>104</sup>, climacteric (female) <sup>105</sup>, conception control <sup>106</sup>, dysmenorrhea <sup>107</sup>, female disorders <sup>108</sup>, habitual abortion <sup>109</sup>, leukoplakia (vulvar) <sup>110</sup>, leukorrhea <sup>111</sup>, menopause <sup>112</sup>, menometrorrhagia <sup>113</sup>, premenstrual <sup>114</sup>, disorders <sup>115</sup>, postpartum bleeding <sup>116</sup>, pregnancy (nausea & vomiting) <sup>117</sup>.

## Infectious Diseases

brucellosis <sup>118</sup>, pneumonia (primary, atypical) <sup>119</sup>, Rocky Mountain spotted fever <sup>120</sup>, tuberculosis <sup>121</sup>.

## Neuromuscular

analgesic <sup>122</sup>, joint and muscle pain <sup>123</sup>, muscle dysfunction <sup>124</sup>, muscle spasm <sup>125</sup>, multiple sclerosis <sup>126</sup>, neuralgia ischiatica <sup>127</sup>, neuritis, diabetic <sup>128</sup>, osseous and neuromuscular disturbances <sup>129</sup>, Parkinsonism <sup>130</sup>.

## Nutrition

anemia <sup>131</sup>, avitaminoses <sup>132</sup>, impaired fat metabolism <sup>133</sup>, malnutrition <sup>134</sup>, mineral deficiencies <sup>135</sup>, obesity <sup>136</sup>, multivitamin deficiencies <sup>137</sup>, pellagra <sup>138</sup>, protein deficiency <sup>139</sup>, vitamin deficiencies <sup>140</sup>, multiple deficiencies <sup>141</sup>.

## Pediatrics

bowel habits <sup>142</sup>, diarrhea <sup>143</sup>, diaper dermatitis <sup>144</sup>, ear infections <sup>145</sup>, formula <sup>146</sup>, infantile eczema, nutritional needs <sup>147</sup>, scurvy <sup>148</sup>.

## Rheumatic and Arthritic Diseases

arthritis <sup>149</sup>, bursitis <sup>150</sup>, gout <sup>151</sup>, gouty arthritis <sup>152</sup>, musculoskeletal pain <sup>153</sup>, rheumatic disease <sup>154</sup>, rheumatic fever <sup>155</sup>, rheumatoid arthritis <sup>156</sup>.

## Miscellaneous

alcoholism <sup>157</sup>, barbiturate poisoning <sup>158</sup>, debridement of necrotic tissue <sup>159</sup>, edema <sup>160</sup>, edema (salt retention) <sup>161</sup>, industrial dermatoses <sup>162</sup>, meningitis <sup>163</sup>, neuropsychiatry <sup>164</sup>, nervous tension <sup>165</sup>, psychoses <sup>166</sup>.



## Prostatectomy

Routine, periodic rectal palpation of the prostate should be done on all men, particularly those 50 years of age and older. Any suspicious area in the prostate should be biopsied. A needle biopsy is of definite value if the limitations of the method are kept in mind.

In cases in which clinical suspicions are grave enough, perineal exposure of the prostate and frozen sections should be made.

Since castration and female hormones do not prolong life, every attempt should be made to carry out radical prostatectomy on all

cases of early carcinoma of the prostate in which the age and general condition of the patient permit.

A series of 12 cases subjected to radical perineal prostatectomy is presented with one operative death and no urinary incontinence or fecal fistula. While each case must be individualized, in general radical prostatic surgery should be limited to those up to 76. The carcinoma should be limited to the prostate, there should be no demonstrable metastases on x-ray and the serum acid and alkaline phosphatase normal.

W. F. Melick and J. J. Naryka, *Missouri Med.*, 50:3, 695, 1955.

## NEW PHARMACEUTICAL PRODUCTS

### Erythrocin 0.2 Gm. Tablets

(Abbott)

Erythromycin, Abbott, *Indications:* pharyngitis, tonsillitis, otitis media, sinusitis, bronchitis, pneumonia, scarlet fever, erysipelas, pyoderma, certain cases of osteomyelitis and other infectious conditions. *Dosage:* Average adult dose is one 0.2 Gm. tablet every 4 to 6 hours. *Supplied:* bottles of 25 and 100 tablets.

### Geriatrone Elixir (U.S. Vitamin)

Nutritional and digestive factors especially designed for the geriatric patient. *Dosage:* One-two table-spoonfuls taken with meals. *Supplied:* bottles of 16 fl. oz.

### Gevrine Capsules (Lederle)

Vitamin, mineral and hormone product. *Indications:* to meet older patients' requirements for vitamins and minerals needed in normal metabolism, and to provide the positive effects on protein and bone maintenance that are produced by the androgen and estrogen hormones. *Dosage:* As directed by physician. *Supplied:* bottles of 100 and 1,000 capsules.

### Cortef Compressed Tablets

(Upjohn)

Each tablet contains hydrocortisone, 10 mg. *Indications:* rheumatoid arthritis. *Dosage:* As directed by physician. *Supplied:* bottles of 25 tablets.

### Darstine Tablets

(Sharp & Dohme)

Mepiperphenidol bromide. Anticholinergic agent. *Indications:* treatment of peptic ulcer and hypermotility of the gastro-intestinal tract. *Dosage:* As directed by physician. *Supplied:* In bottles of 50 mg. tablets.

### Quelicin Chloride Solution

(Abbott)

Succinylcholine chloride. *Indications:* production of muscular relaxation to facilitate endotracheal intubation, endoscopic examination and orthopedic manipulation and providing relaxation for general surgical procedures. *Dosage:* Initial dose of 20 mg. recommended. *Supplied:* In 10 cc. multiple-dose vials containing 20 mg. per cc. in 10 cc. ampuls containing 50 mg. per cc.

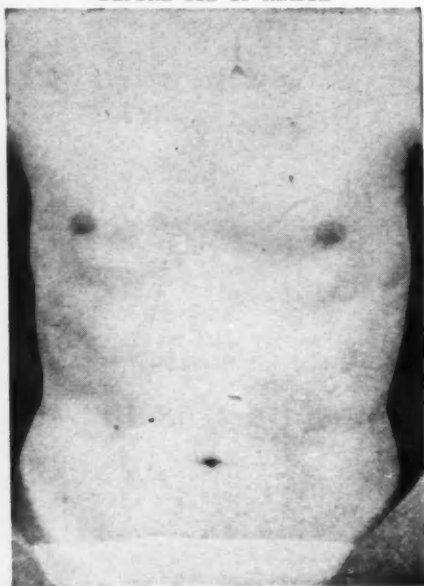
### Achromycin

(Lederle)

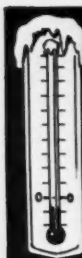
New antibiotic, tetracycline. *Indication:* beta hemolytic streptococcal infections, E. coli infections (including urinary tract infections, peritonitis, abscesses), meningococcal, staphylococcal, pneumococcal and gonococcal infections, otitis media and mastoiditis, acute bronchitis and bronchiolitis, actinomycosis, and spine viral and rickettsial diseases. *Dosage:* As directed by physician. *Supplied:* In 250 mg., 100 mg. and 50 mg. capsules. Spersoids, 50 mg. per teaspoonful (3.0 Gm.), Intravenous, 500 mg., 250 mg., and 100 mg.



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